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(54) Title: NUCLEIC ACID MOLECULES ENCODING PROTEINS ESSENTIAL FOR PLANT GROWTH AND DEVELOPMENT AND USES THEREOF

(57) Abstract: Nucleotide sequences are isolated from Arabidopsis thaliana that code for proteins essential for plant growth and development. The essentially of the proteins may be exploited by recombinantly expressing the proteins and using them in screening assays to identify compounds that interact with or inhibit the proteins and are therefore potential herbicides.



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NUCLEIC ACID MOLECULES ENCODING PROTEINS ESSENTIAL FOR PLANT GROWTH AND DEVELOPMENT AND USES THEREOF

The present invention pertains to nucleic acid molecules isolated from Arabidopsis thaliana comprising nucleotide sequences that encode proteins essential for plant growth and development. The invention particularly relates to methods of using these proteins as herbicide targets, based on this essentiality.

The use of herbicides to control undesirable vegetation such as weeds in crop fields has become almost a universal practice. The herbicide market exceeds 15 billion dollars annually. Despite this extensive use, weed control remains a significant and costly problem for farmers.

method of application and stage of weed plant development are critical to achieving good weed control with herbicides. Because various weed species are resistant to herbicides, the production of effective new herbicides becomes increasingly important. New herbicides can now be discovered using high-throughput screens that implement recombinant DNA technology. Metabolic enzymes found to be essential to plant growth and development can be recombinantly produced through standard molecular biological techniques and utilized as herbicide targets in screens for novel inhibitors of the enzyme activity. More generally, any essential plant protein can be used to screen for inhibitors of its activity. The novel inhibitors discovered through such screens may then be used as herbicides to control undesirable vegetation.

In view of the above, there remain persistent and ongoing problems with unwanted or detrimental vegetation growth (e.g. weeds). Furthermore, as the population continues to grow, there will be increasing food shortages. Therefore, there exists a long felt, yet unfulfilled need, to find new, effective, and economic herbicides.

In view of these needs, it is an object of the invention to provide nucleic acid molecules from Arabidopsis thaliana comprising nucleotide sequences that encode proteins essential for plant growth and development. It is another object to provide the essential proteins encoded by these essential nucleotide sequences for assay development to identify

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inhibitory compounds with herbicidal activity. It is still another object of the present invention to provide an effective and beneficial method for identifying new or improved herbicides using the essential proteins of the invention.

In furtherance of these and other objects, the present invention provides nucleic acid molecules isolated from Arabidopsis thaliana comprising nucleotide sequences that encode proteins essential for plant viability. Genetic results show that when any of the nucleotide sequences of the invention are mutated in Arabidopsis thaliana, the resulting phenotype is embryo or seedling lethal in the homozygous state. In particular, by using Ac/Ds transposon or T-DNA-mediated mutagenesis, the inventors of the present invention are the first to demonstrate that the activity of each protein of the present invention is essential for plant growth in Arabidopsis thaliana.

This knowledge is exploited to provide novel herbicide modes of action. The critical role in plant growth of the proteins encoded by each of the nucleotide sequences of the invention implies that chemicals that inhibit the function of any one of these proteins in plants are likely to have detrimental effects on plants and are potentially good herbicide candidates. Thus, the proteins encoded by the essential nucleotide sequences provide the bases for assays designed to easily and rapidly identify novel herbicides.

The present invention therefore provides methods of using a purified protein encoded by any one of the nucleotide sequences described below to identify inhibitors thereof, which can then be used as herbicides to suppress the growth of undesirable vegetation, e.g. in fields where crops are grown, particularly agronomically important crops such as maize and other cereal crops such as wheat, oats, rye, sorghum, rice, barley, millet, turf and forage grasses, and the like, as well as cotton, sugar cane, sugar beet, oilseed rape, and soybeans.

Disclosed herein are nucleic acid molecules isolated from Arabidopsis thaliana. In one embodiment, the present invention provides an isolated nucleic acid molecule comprising a nucleotide sequence, the complement of which hybridizes under stringent conditions to a sequence selected from the group consisting of the odd numbered SEQ ID NOs:1-95. In another embodiment, the present invention provides an isolated nucleic acid molecule comprising a nucleotide sequence that encodes a protein comprising an amino acid sequence having at least 60%, preferably 70%, more preferably 80%, still more preferably 90%, even more preferably 95%, and most preferably 99-100% sequence identity to an amino acid sequence selected from the group consisting of the even numbered SEQ ID NOs:2-96.

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The present invention also provides a chimeric construct comprising a promoter operatively linked to a nucleic acid molecule according to the present invention, wherein the promoter is preferably functional in a eukaryote, wherein the promoter is preferably heterologous to the nucleic acid molecule. The present invention further provides a recombinant vector comprising a chimeric construct according to the present invention, wherein said vector is capable of being stably transformed into a host cell. The present invention still further provides a host cell comprising a nucleic acid molecule according to the present invention, wherein said nucleic acid molecule is preferably expressible in the cell. The host cell is preferably selected from the group consisting of a plant cell, a yeast cell, an insect cell, and a prokaryotic cell. The present invention additionally provides a plant or seed comprising a plant cell according to the present invention.

The present invention also provides proteins essential for plant growth in Arabidopsis thaliana. In one embodiment, the present invention provides an isolated protein comprising an amino acid sequence having at least 60%, preferably 70%, more preferably 80%, still more preferably 90%, even more preferably 95%, and most preferably 99-100% sequence identity to an amino acid sequence selected from the group consisting of the even numbered SEQ ID NOs:2-96. In accordance with another embodiment, the present invention also relates to the recombinant production of proteins of the invention and methods of using the proteins of the invention in assays for identifying compounds that interact with the protein.

According to another aspect, the present invention provides a method of identifying a herbicidal compound, comprising: (a) combining a polypeptide comprising an amino acid sequence at least 90% identical to an amino acid sequence selected from the group consisting of the even numbered SEQ ID NOs:2-96 with a compound to be tested for the ability to bind to said polypeptide, under conditions conducive to binding; (b) selecting a compound identified in (a) that binds to said polypeptide; (c) applying a compound selected in (b) to a plant to test for herbicidal activity; and (d) selecting a compound identified in (c) that has herbicidal activity. Preferably, the polypeptide comprises an amino acid sequence at least 95% identical to an amino acid sequence selected from the group consisting of the even numbered SEQ ID NOs:2-96. More preferably, the polypeptide comprises an amino acid sequence at least 99% identical to an amino acid sequence selected from the group consisting of the even numbered SEQ ID NOs:2-96. Most preferably, the polypeptide comprises an amino acid sequence selected from the group consisting of the even numbered SEQ ID NOs:2-96. Most preferably, the polypeptide comprises an amino acid sequence selected from the group consisting of the even numbered SEQ ID

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NOs:2-96. The present invention also provides a method for killing or inhibiting the growth or viability of a plant, comprising applying to the plant a herbicidal compound identified according to this method.

According to yet another aspect, the present invention provides a method of identifying a herbicidal compound, comprising: (a) combining a polypeptide comprising an amino acid sequence at least 90% identical to an amino acid sequence selected from the group consisting of the even numbered SEQ ID NOs:2-96 with a compound to be tested for the ability to inhibit the activity of said polypeptide, under conditions conducive to inhibition; (b) selecting a compound identified in (a) that inhibits the activity of said polypeptide; (c) applying a compound selected in (b) to a plant to test for herbicidal activity; and (d) selecting a compound identified in (c) that has herbicidal activity. Preferably, the polypeptide comprises an amino acid sequence at least 95% identical to an amino acid sequence selected from the group consisting of the even numbered SEQ ID NOs:2-96. More preferably, the polypeptide comprises an amino acid sequence at least 99% identical to an amino acid sequence selected from the group consisting of the even numbered SEQ ID NOs:2-96. Most preferably, the polypeptide comprises an amino acid sequence selected from the group consisting of the even numbered SEQ ID NOs:2-96. The present invention also provides a method for killing or inhibiting the growth or viability of a plant, comprising applying to the plant a herbicidal compound identified according to this method.

The present invention still further provides a method for killing or inhibiting the growth or viability of a plant, comprising inhibiting expression in said plant of a protein having at least 60%, preferably 70%, more preferably 80%, still more preferably 90%, even more preferably 95%, and most preferably 99-100% sequence identity to an amino acid sequence selected from the group consisting of the even numbered SEQ ID NOs:2-96.

Other objects and advantages of the present invention will become apparent to those skilled in the art and from a study of the following description of the invention and non-limiting examples. The entire contents of all publications mentioned herein are hereby incorporated by reference.

BRIEF DESCRIPTION OF THE SEQUENCES IN THE SEQUENCE LISTING

Odd numbered SEQ ID NOs:1-95 are nucleotide sequences isolated from

Arabidopsis thaliana that are more fully described in Table 5 below.

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Even numbered SEQ ID NOs:2-96 are protein sequences encoded by the immediately preceding nucleotide sequence, e.g., SEQ ID NO:2 is the protein encoded by the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:4 is the protein encoded by the nucleotide sequence of SEQ ID NO:3, etc.

SEQ ID NOs:101-125 are PCR primers.

DEFINITIONS

For clarity, certain terms used in the specification are defined and presented as follows:

"Associated with / operatively linked" refer to two nucleic acid sequences that are related physically or functionally. For example, a promoter or regulatory DNA sequence is said to be "associated with" a DNA sequence that codes for an RNA or a protein if the two sequences are operatively linked, or situated such that the regulator DNA sequence will affect the expression level of the coding or structural DNA sequence.

A "chimeric construct" is a recombinant nucleic acid sequence in which a promoter or regulatory nucleic acid sequence is operatively linked to, or associated with, a nucleic acid sequence that codes for an mRNA or which is expressed as a protein, such that the regulatory nucleic acid sequence is able to regulate transcription or expression of the associated nucleic acid sequence. The regulatory nucleic acid sequence of the chimeric construct is not normally operatively linked to the associated nucleic acid sequence as found in nature.

Co-factor: natural reactant, such as an organic molecule or a metal ion, required in an enzyme-catalyzed reaction. A co-factor is *e.g.* NAD(P), riboflavin (including FAD and FMN), folate, molybdopterin, thiamin, biotin, lipoic acid, pantothenic acid and coenzyme A, S-adenosylmethionine, pyridoxal phosphate, ubiquinone, menaquinone. Optionally, a co-factor can be regenerated and reused.

A "coding sequence" is a nucleic acid sequence that is transcribed into RNA such as mRNA, rRNA, tRNA, snRNA, sense RNA or antisense RNA. Preferably the RNA is then translated in an organism to produce a protein.

Complementary: "complementary" refers to two nucleotide sequences that comprise antiparallel nucleotide sequences capable of pairing with one another upon formation of hydrogen bonds between the complementary base residues in the antiparallel nucleotide sequences.

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Enzyme activity: means herein the ability of an enzyme to catalyze the conversion of a substrate into a product. A substrate for the enzyme comprises the natural substrate of the enzyme but also comprises analogues of the natural substrate, which can also be converted, by the enzyme into a product or into an analogue of a product. The activity of the enzyme is measured for example by determining the amount of product in the reaction after a certain period of time, or by determining the amount of substrate remaining in the reaction mixture after a certain period of time. The activity of the enzyme is also measured by determining the amount of an unused co-factor of the reaction remaining in the reaction mixture after a certain period of time or by determining the amount of used co-factor in the reaction mixture after a certain period of time. The activity of the enzyme is also measured by determining the amount of a donor of free energy or energy-rich molecule (e.g. ATP, phosphoenolpyruvate, acetyl phosphate or phosphocreatine) remaining in the reaction mixture after a certain period of time or by determining the amount of a used donor of free energy or energy-rich molecule (e.g. ADP, pyruvate, acetate or creatine) in the reaction mixture after a certain period of time.

Essential: an "essential" Arabidopsis thaliana nucleotide sequence is a nucleotide sequence encoding a protein such as e.g. a biosynthetic enzyme, receptor, signal transduction protein, structural gene product, or transport protein that is essential to the growth or survival of the plant.

Expression Cassette: "Expression cassette" as used herein means a nucleic acid molecule capable of directing expression of a particular nucleotide sequence in an appropriate host cell, comprising a promoter operatively linked to the nucleotide sequence of interest which is operatively linked to termination signals. It also typically comprises sequences required for proper translation of the nucleotide sequence. The coding region usually codes for a protein of interest but may also code for a functional RNA of interest, for example antisense RNA or a nontranslated RNA, in the sense or antisense direction. The expression cassette comprising the nucleotide sequence of interest may be chimeric, meaning that at least one of its components is heterologous with respect to at least one of its other components. The expression cassette may also be one that is naturally occurring but has been obtained in a recombinant form useful for heterologous expression. Typically, however, the expression cassette is heterologous with respect to the host, i.e., the particular DNA sequence of the expression cassette does not occur naturally in the host cell and must have been introduced into the host cell or an ancestor of the host cell by a transformation event. The expression of

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the nucleotide sequence in the expression cassette may be under the control of a constitutive promoter or of an inducible promoter that initiates transcription only when the host cell is exposed to some particular external stimulus. In the case of a multicellular organism, such as a plant, the promoter can also be specific to a particular tissue or organ or stage of development.

Gene: the term "gene" is used broadly to refer to any segment of DNA associated with a biological function. Thus, genes include coding sequences and/or the regulatory sequences required for their expression. Genes also include nonexpressed DNA segments that, for example, form recognition sequences for other proteins. Genes can be obtained from a variety of sources, including cloning from a source of interest or synthesizing from known or predicted sequence information, and may include sequences designed to have desired parameters.

Heterologous/exogenous: The terms "heterologous" and "exogenous" when used herein to refer to a nucleic acid sequence (e.g. a DNA sequence) or a gene, refer to a sequence that originates from a source foreign to the particular host cell or, if from the same source, is modified from its original form. Thus, a heterologous gene in a host cell includes a gene that is endogenous to the particular host cell but has been modified through, for example, the use of DNA shuffling. The terms also include non-naturally occurring multiple copies of a naturally occurring DNA sequence. Thus, the terms refer to a DNA segment that is foreign or heterologous to the cell, or homologous to the cell but in a position within the host cell nucleic acid in which the element is not ordinarily found. Exogenous DNA segments are expressed to yield exogenous polypeptides.

A "homologous" nucleic acid (e.g. DNA) sequence is a nucleic acid (e.g. DNA) sequence naturally associated with a host cell into which it is introduced.

Hybridization: The phrase "hybridizing specifically to" refers to the binding, duplexing, or hybridizing of a molecule only to a particular nucleotide sequence under stringent conditions when that sequence is present in a complex mixture (e.g., total cellular) DNA or RNA. "Bind(s) substantially" refers to complementary hybridization between a probe nucleic acid and a target nucleic acid and embraces minor mismatches that can be accommodated by reducing the stringency of the hybridization media to achieve the desired detection of the target nucleic acid sequence.

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Inhibitor: a chemical substance that inactivates the enzymatic activity of a protein such as a biosynthetic enzyme, receptor, signal transduction protein, structural gene product, or transport protein. The term "herbicide" (or "herbicidal compound") is used herein to define an inhibitor applied to a plant at any stage of development, whereby the herbicide inhibits the growth of the plant or kills the plant.

Interaction: quality or state of mutual action such that the effectiveness or toxicity of one protein or compound on another protein is inhibitory (antagonists) or enhancing (agonists).

A nucleic acid sequence is "isocoding with" a reference nucleic acid sequence when the nucleic acid sequence encodes a polypeptide having the same amino acid sequence as the polypeptide encoded by the reference nucleic acid sequence.

Isogenic: plants that are genetically identical, except that they may differ by the presence or absence of a heterologous DNA sequence.

Isolated: in the context of the present invention, an isolated DNA molecule or an isolated enzyme is a DNA molecule or enzyme that, by the hand of man, exists apart from its native environment and is therefore not a product of nature. An isolated DNA molecule or enzyme may exist in a purified form or may exist in a non-native environment such as, for example, in a transgenic host cell.

Mature protein: protein from which the transit peptide, signal peptide, and/or propeptide portions have been removed.

Minimal Promoter: the smallest piece of a promoter, such as a TATA element, that can support any transcription. A minimal promoter typically has greatly reduced promoter activity in the absence of upstream activation. In the presence of a suitable transcription factor, the minimal promoter functions to permit transcription.

Modified Enzyme Activity: enzyme activity different from that which naturally occurs in a plant (i.e. enzyme activity that occurs naturally in the absence of direct or indirect manipulation of such activity by man), which is tolerant to inhibitors that inhibit the naturally occurring enzyme activity.

Naturally occurring: the term "naturally occurring" is used to describe an object that can be found in nature as distinct from being artificially produced by man. For example, a protein or nucleotide sequence present in an organism (including a virus), which can be

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isolated from a source in nature and which has not been intentionally modified by man in the laboratory, is naturally occurring.

Nucleic acid: the term "nucleic acid" refers to deoxyribonucleotides or ribonucleotides and polymers thereof in either single- or double-stranded form. Unless specifically limited, the term encompasses nucleic acids containing known analogues of natural nucleotides which have similar binding properties as the reference nucleic acid and are metabolized in a manner similar to naturally occurring nucleotides. Unless otherwise indicated, a particular nucleic acid sequence also implicitly encompasses conservatively modified variants thereof (e.g. degenerate codon substitutions) and complementary sequences and as well as the sequence explicitly indicated. Specifically, degenerate codon substitutions may be achieved by generating sequences in which the third position of one or more selected (or all) codons is substituted with mixed-base and/or deoxyinosine residues (Batzer et al., Nucleic Acid Res. 19: 5081 (1991); Ohtsuka et al., J. Biol. Chem. 260: 2605-2608 (1985); Rossolini et al., Mol. Cell. Probes 8: 91-98 (1994)). The terms "nucleic acid" or "nucleic acid sequence" may also be used interchangeably with gene, cDNA, and mRNA encoded by a gene.

"ORF" means open reading frame.

Percent identity: the phrases "percent identical" or "percent identical," in the context of two nucleic acid or protein sequences, refers to two or more sequences or subsequences that have for example 60%, preferably 70%, more preferably 80%, still more preferably 90%, even more preferably 95%, and most preferably at least 99% nucleotide or amino acid residue identity, when compared and aligned for maximum correspondence, as measured using one of the following sequence comparison algorithms or by visual inspection. Preferably, the percent identity exists over a region of the sequences that is at least about 50 residues in length, more preferably over a region of at least about 100 residues, and most preferably the percent identity exists over at least about 150 residues. In an especially preferred embodiment, the percent identity exists over the entire length of the coding regions.

For sequence comparison, typically one sequence acts as a reference sequence to which test sequences are compared. When using a sequence comparison algorithm, test and reference sequences are input into a computer, subsequence coordinates are designated if necessary, and sequence algorithm program parameters are designated. The sequence comparison algorithm then calculates the percent sequence identity for the test sequence(s) relative to the reference sequence, based on the designated program parameters.

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Optimal alignment of sequences for comparison can be conducted, e.g., by the local homology algorithm of Smith & Waterman, Adv. Appl. Math. 2: 482 (1981), by the homology alignment algorithm of Needleman & Wunsch, J. Mol. Biol. 48: 443 (1970), by the search for similarity method of Pearson & Lipman, Proc. Nat'l. Acad. Sci. USA 85: 2444 (1988), by computerized implementations of these algorithms (GAP, BESTFIT, FASTA, and TFASTA in the Wisconsin Genetics Software Package, Genetics Computer Group, 575 Science Dr., Madison, WI), or by visual inspection (see generally, Ausubel et al., infra).

One example of an algorithm that is suitable for determining percent sequence identity and sequence similarity is the BLAST algorithm, which is described in Altschul et al., J. Mol. Biol. 215: 403-410 (1990). Software for performing BLAST analyses is publicly available through the National Center for Biotechnology Information (http://www.ncbi.nlm.nih.gov/). This algorithm involves first identifying high scoring sequence pairs (HSPs) by identifying short words of length W in the query sequence, which either match or satisfy some positive-valued threshold score T when aligned with a word of the same length in a database sequence. T is referred to as the neighborhood word score threshold (Altschul et al., 1990). These initial neighborhood word hits act as seeds for initiating searches to find longer HSPs containing them. The word hits are then extended in both directions along each sequence for as far as the cumulative alignment score can be increased. Cumulative scores are calculated using, for nucleotide sequences, the parameters M (reward score for a pair of matching residues; always > 0) and N (penalty score for mismatching residues; always < 0). For amino acid sequences, a scoring matrix is used to calculate the cumulative score. Extension of the word hits in each direction are halted when the cumulative alignment score falls off by the quantity X from its maximum achieved value, the cumulative score goes to zero or below due to the accumulation of one or more negative-scoring residue alignments, or the end of either sequence is reached. The BLAST algorithm parameters W, T, and X determine the sensitivity and speed of the alignment. The BLASTN program (for nucleotide sequences) uses as defaults a wordlength (W) of 11, an expectation (E) of 10, a cutoff of 100, M=5, N=-4, and a comparison of both strands. For amino acid sequences, the BLASTP program uses as defaults a wordlength (W) of 3, an expectation (E) of 10, and the BLOSUM62 scoring matrix (see Henikoff & Henikoff, Proc. Natl. Acad. Sci. USA 89: 10915 (1989)).

In addition to calculating percent sequence identity, the BLAST algorithm also performs a statistical analysis of the similarity between two sequences (see, e.g., Karlin &

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Altschul, *Proc. Nat'l. Acad. Sci. USA* 90: 5873-5787 (1993)). One measure of similarity provided by the BLAST algorithm is the smallest sum probability (P(N)), which provides an indication of the probability by which a match between two nucleotide or amino acid sequences would occur by chance. For example, a test nucleic acid sequence is considered similar to a reference sequence if the smallest sum probability in a comparison of the test nucleic acid sequence to the reference nucleic acid sequence is less than about 0.1, more preferably less than about 0.01, and most preferably less than about 0.001.

Pre-protein: protein that is normally targeted to a cellular organelle, such as a chloroplast, and still comprises its native transit peptide.

Purified: the term "purified," when applied to a nucleic acid or protein, denotes that the nucleic acid or protein is essentially free of other cellular components with which it is associated in the natural state. It is preferably in a homogeneous state although it can be in either a dry or aqueous solution. Purity and homogeneity are typically determined using analytical chemistry techniques such as polyacrylamide gel electrophoresis or high performance liquid chromatography. A protein that is the predominant species present in a preparation is substantially purified. The term "purified" denotes that a nucleic acid or protein gives rise to essentially one band in an electrophoretic gel. Particularly, it means that the nucleic acid or protein is at least about 50% pure, more preferably at least about 85% pure, and most preferably at least about 99% pure.

Two nucleic acids are "recombined" when sequences from each of the two nucleic acids are combined in a progeny nucleic acid. Two sequences are "directly" recombined when both of the nucleic acids are substrates for recombination. Two sequences are "indirectly recombined" when the sequences are recombined using an intermediate such as a cross-over oligonucleotide. For indirect recombination, no more than one of the sequences is an actual substrate for recombination, and in some cases, neither sequence is a substrate for recombination.

"Regulatory elements" refer to sequences involved in controlling the expression of a nucleotide sequence. Regulatory elements comprise a promoter operatively linked to the nucleotide sequence of interest and termination signals. They also typically encompass sequences required for proper translation of the nucleotide sequence.

Significant Increase: an increase in enzymatic activity that is larger than the margin of error inherent in the measurement technique, preferably an increase by about 2-fold or greater

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of the activity of the wild-type enzyme in the presence of the inhibitor, more preferably an increase by about 5-fold or greater, and most preferably an increase by about 10-fold or greater.

Significantly less: means that the amount of a product of an enzymatic reaction is reduced by more than the margin of error inherent in the measurement technique, preferably a decrease by about 2-fold or greater of the activity of the wild-type enzyme in the absence of the inhibitor, more preferably an decrease by about 5-fold or greater, and most preferably an decrease by about 10-fold or greater.

Specific Binding/Immunological Cross-Reactivity: An indication that two nucleic acid sequences or proteins are substantially identical is that the protein encoded by the first nucleic acid is immunologically cross reactive with, or specifically binds to, the protein encoded by the second nucleic acid. Thus, a protein is typically substantially identical to a second protein, for example, where the two proteins differ only by conservative substitutions. The phrase "specifically (or selectively) binds to an antibody," or "specifically (or selectively) immunoreactive with," when referring to a protein or peptide, refers to a binding reaction which is determinative of the presence of the protein in the presence of a heterogeneous population of proteins and other biologics. Thus, under designated immunoassay conditions, the specified antibodies bind to a particular protein and do not bind in a significant amount to other proteins present in the sample. Specific binding to an antibody under such conditions may require an antibody that is selected for its specificity for a particular protein. For example, antibodies raised to the protein with the amino acid sequence encoded by any of the nucleic acid sequences of the invention can be selected to obtain antibodies specifically immunoreactive with that protein and not with other proteins except for polymorphic variants. A variety of immunoassay formats may be used to select antibodies specifically immunoreactive with a particular protein. For example, solid-phase ELISA immunoassays, Western blots, or immunohistochemistry are routinely used to select monoclonal antibodies specifically immunoreactive with a protein. See Harlow and Lane (1988) Antibodies, A Laboratory Manual, Cold Spring Harbor Publications, New York "Harlow and Lane"), for a description of immunoassay formats and conditions that can be used to determine specific immunoreactivity. Typically a specific or selective reaction will be at least twice background signal or noise and more typically more than 10 to 100 times background.

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"Stringent hybridization conditions" and "stringent hybridization wash conditions" in the context of nucleic acid hybridization experiments such as Southern and Northern hybridizations are sequence dependent, and are different under different environmental parameters. Longer sequences hybridize specifically at higher temperatures. An extensive guide to the hybridization of nucleic acids is found in Tijssen (1993) *Laboratory Techniques in Biochemistry and Molecular Biology-Hybridization with Nucleic* Acid Probes part I chapter 2 "Overview of principles of hybridization and the strategy of nucleic acid probe assays" Elsevier, New York. Generally, highly stringent hybridization and wash conditions are selected to be about 5°C lower than the thermal melting point (T_m) for the specific sequence at a defined ionic strength and pH. Typically, under "stringent conditions" a probe will hybridize to its target subsequence, but to no other sequences.

The T_m is the temperature (under defined ionic strength and pH) at which 50% of the target sequence hybridizes to a perfectly matched probe. Very stringent conditions are selected to be equal to the T_m for a particular probe. An example of stringent hybridization conditions for hybridization of complementary nucleic acids which have more than 100 complementary residues on a filter in a Southern or northern blot is 50% formamide with 1 mg of heparin at 42°C, with the hybridization being carried out overnight. An example of highly stringent wash conditions is 0.1 5M NaCl at 72°C for about 15 minutes. An example of stringent wash conditions is a 0.2x SSC wash at 65°C for 15 minutes (see, Sambrook, infra, for a description of SSC buffer). Often, a high stringency wash is preceded by a low stringency wash to remove background probe signal. An example medium stringency wash for a duplex of, e.g., more than 100 nucleotides, is 1x SSC at 45°C for 15 minutes. An example low stringency wash for a duplex of, e.g., more than 100 nucleotides, is 4-6x SSC at 40°C for 15 minutes. For short probes (e.g., about 10 to 50 nucleotides), stringent conditions typically involve salt concentrations of less than about 1.0 M Na ion, typically about 0.01 to 1.0 M Na ion concentration (or other salts) at pH 7.0 to 8.3, and the temperature is typically at least about 30°C. Stringent conditions can also be achieved with the addition of destabilizing agents such as formamide. In general, a signal to noise ratio of 2x (or higher) than that observed for an unrelated probe in the particular hybridization assay indicates detection of a specific hybridization. Nucleic acids that do not hybridize to each other under stringent conditions are still substantially identical if the proteins that they encode are substantially

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identical. This occurs, e.g., when a copy of a nucleic acid is created using the maximum codon degeneracy permitted by the genetic code.

The following are examples of sets of hybridization/wash conditions that may be used to clone nucleotide sequences that are homologues of reference nucleotide sequences of the present invention: a reference nucleotide sequence preferably hybridizes to the reference nucleotide sequence in 7% sodium dodecyl sulfate (SDS), 0.5 M NaPO₄, 1 mM EDTA at 50°C with washing in 2X SSC, 0.1% SDS at 50°C, more desirably in 7% sodium dodecyl sulfate (SDS), 0.5 M NaPO₄, 1 mM EDTA at 50°C with washing in 1X SSC, 0.1% SDS at 50°C, more desirably still in 7% sodium dodecyl sulfate (SDS), 0.5 M NaPO₄, 1 mM EDTA at 50°C with washing in 0.5X SSC, 0.1% SDS at 50°C, preferably in 7% sodium dodecyl sulfate (SDS), 0.5 M NaPO₄, 1 mM EDTA at 50°C, more preferably in 7% sodium dodecyl sulfate (SDS), 0.5 M NaPO₄, 1 mM EDTA at 50°C, with washing in 0.1X SSC, 0.1% SDS at 50°C, with washing in 0.1X SSC, 0.1% SDS at 50°C with washing in 0.1X SSC, 0.1% SDS at 50°C.

A "subsequence" refers to a sequence of nucleic acids or amino acids that comprise a part of a longer sequence of nucleic acids or amino acids (e.g., protein) respectively.

Substrate: a substrate is the molecule that an enzyme naturally recognizes and converts to a product in the biochemical pathway in which the enzyme naturally carries out its function, or is a modified version of the molecule, which is also recognized by the enzyme and is converted by the enzyme to a product in an enzymatic reaction similar to the naturally-occurring reaction.

Transformation: a process for introducing heterologous DNA into a plant cell, plant tissue, or plant. Transformed plant cells, plant tissue, or plants are understood to encompass not only the end product of a transformation process, but also transgenic progeny thereof.

"Transformed," "transgenic," and "recombinant" refer to a host organism such as a bacterium or a plant into which a heterologous nucleic acid molecule has been introduced. The nucleic acid molecule can be stably integrated into the genome of the host or the nucleic acid molecule can also be present as an extrachromosomal molecule. Such an extrachromosomal molecule can be auto-replicating. Transformed cells, tissues, or plants are understood to encompass not only the end product of a transformation process, but also transgenic progeny thereof. A "non-transformed," "non-transgenic," or "non-recombinant" host refers to a wild-type organism, e.g., a bacterium or plant, which does not contain the heterologous nucleic acid molecule.

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Viability: "viability" as used herein refers to a fitness parameter of a plant. Plants are assayed for their homozygous performance of plant development, indicating which proteins are essential for plant growth.

5 I. Identification of Essential Arabidopsis thaliana Nucleotide Sequences and Encoded Proteins Using Ac/Ds Transposon or T-DNA-Mediated Mutagenesis

As shown in the examples below, the essentiality of the nucleotide sequences described herein for normal plant growth and development, have been demonstrated for the first time in *Arabidopsis* using *Ac/Ds* transposon or T-DNA-mediated mutagenesis. Having established the essentiality of the function of the encoded proteins in *Arabidopsis thaliana* and having identified the nucleotide sequences encoding these essential proteins, the inventors thereby provide an important and sought after tool for new herbicide development.

Arabidopsis insertional mutant lines segregating for seedling lethal mutations are identified as a first step in the identification of essential proteins. Starting with T2 seeds collected from single T1 plants containing T-DNA insertions in their genomes, those lines segregating homozygous seedling lethal seedlings are identified. Ds transposon insertion lines are produced as described in Sundaresan et al. (1995) (Genes and Dev., 9:1797-1810), incorporated herein by reference. Starting with F3 or F4 seeds collected from single F2 or F3 kanamycin-resistant plants containing Ds insertions in their genomes (see Figure 3 of Sundaresan et al. (1995) (Genes and Dev., 9:1797-1810), those lines segregating homozygous seedling lethal seedlings are identified. These lines are found by placing seeds onto minimal plant growth media, which contains the fungicides benomyl and maxim, and screening for inviable seedlings after 7 and 14 days in the light at room temperature. Inviable phenotypes include altered pigmentation or altered morphology. These phenotypes are observed either on plates directly or in soil following transplantation of seedlings.

Essential genes are also identified through the isolation of lethal mutants blocked in early development. Examples of lethal mutants include those blocked in the formation of the male or female gametes or embryo. Gametophytic mutants are found by examining T1 insertion lines for the presence of 50% aborted pollen grains or ovules. Embryo defective mutants produce 25% defective seeds following self-pollination of T1 plants (see Errampalli et al. 1991, Plant Cell 3:149-157; Castle et al. 1993, Mol Gen Genet 241:504-514).

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When a line is identified as segregating a seedling lethal or an embryo defective phenotype, it is determined if the resistance marker in the *Ds* transposon or T-DNA insertion co-segregates with the lethality (Errampalli *et al.* (1991) The Plant Cell, 3:149-157). Cosegregation analysis is done by placing the seeds on media containing the selective agent and scoring the seedlings for resistance or sensitivity to the agent. Examples of selective agents used are kanamycin, hygromycin, or phosphinothricin. About 35 resistant seedlings are transplanted to soil and their progeny are examined for the segregation of the seedling lethal. In the case in which the *Ds* transposon or T-DNA insertion disrupts an essential gene, there is co-segregation of the resistance phenotype and the seedling lethal or embryo defective phenotype in every plant. Therefore, in such a case, all resistant plants segregate a seedling lethal or embryo defective phenotype in the next generation; this result indicates that each of the resistant plants is heterozygous for the mutation and hemizygous for the T-DNA insert causing the mutation.

For the Arabidopsis lines showing co-segregation of the transposon-encoded or T-DNA-encoded resistance marker and the lethal phenotype, PCR-based molecular approaches such as, TAIL-PCR (Liu et al. (1995) Plant J., 8:457-463; Liu and Whittier (1995), Genomics, 25:674-681), TAIL2k, vectorette PCR (Riley et al. (1990) Nucleic Acids Research, 18: 2887-2890), or the GenomeWalker™ kit (CLONTECH Laboratories, Inc., Palo Alto, CA), may be used to directly amplify the plant DNA fragments flanking the transposon or T-DNA. Each of these techniques utilizes the known sequence of the transposon or T-DNA, and can be used to recover small (less than 5 kb) fragments directly adjacent to the insertion. PCR products are isolated and their DNA sequence is determined.

Alternatively, plasmid rescue may be used to isolate the plant DNA/T-DNA border fragments. Southern blot analysis may be performed as an initial step in the characterization of the molecular nature of each insertion. Southern blots are done with genomic DNA isolated from heterozygotes and using probes capable of hybridizing with the T-DNA vector DNA. Using the results of the Southern analysis, appropriate restriction enzymes are chosen to perform plasmid rescue in order to molecularly clone *Arabidopsis thaliana* genomic DNA flanking one or both sides of the T-DNA insertion. Plasmids obtained in this manner are analyzed by restriction enzyme digestion to sort the plasmids into classes based on their digestion pattern. For each class of plasmid clone, the DNA sequence is determined.

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The resulting sequences, obtained by any of the above outlined approaches, are analyzed for the presence of non-Ds transposon and non-T-DNA vector sequences, as appropriate. When such sequences are found, they are used to search DNA and protein databases using the BLAST and BLAST2 programs (Altschul et al. (1990) J Mol. Biol. 215: 403-410; Altschul et al. (1997) Nucleic Acid Res. 25:3389-3402, both incorporated herein by reference). Additional genomic and cDNA sequences for each gene are identified by standard molecular biology procedures.

II. Recombinant Production Of Essential Proteins And Uses Thereof

For recombinant production of a protein of the invention in a host organism, a nucleotide sequence encoding the protein is inserted into an expression cassette designed for the chosen host and introduced into the host where it is recombinantly produced. The choice of the specific regulatory sequences such as promoter, signal sequence, 5' and 3' untranslated sequence, and enhancer appropriate for the chosen host is within the level of the skill of the routineer in the art. The resultant molecule, containing the individual elements linking in the proper reading frame, is inserted into a vector capable of being transformed into the host cell. Suitable expression vectors and methods for recombinant production of proteins are well known for host organisms such as *E. coli*, yeast, and insect cells (see, *e.g.*, Lucknow and Summers, *Bio/Technol.* 6:47 (1988)). Additional suitable expression vectors are baculovirus expression vectors, *e.g.*, those derived from the genome of *Autographica californica* nuclear polyhedrosis virus (AcMNPV). A preferred baculovirus/insect system is PVL1392(3) used to transfect *Spodoptera frugiperda* SF9 cells (ATCC) in the presence of linear *Autographica californica* baculovirus DNA (Phramingen, San Diego, CA). The resulting virus is used to infect HighFive *Tricoplusia ni* cells (Invitrogen, La Jolla, CA).

Recombinantly produced proteins are isolated and purified using a variety of standard techniques. The actual techniques used vary depending upon the host organism used, whether the protein is designed for secretion, and other such factors. Such techniques are well known to the skilled artisan (see, e.g. chapter 16 of Ausubel, F. et al., "Current Protocols in Molecular Biology", pub. by John Wiley & Sons, Inc. (1994).

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III. Assays For Characterizing The Essential Proteins

The recombinantly produced proteins described herein are useful for a variety of purposes. For example, they can be used in *in vitro* assays to screen known herbicidal chemicals whose target has not been identified to determine if they inhibit protein activity. Such *in vitro* assays may also be used as more general screens to identify chemicals that inhibit such protein activity and that are therefore novel herbicide candidates. Recombinantly produced proteins may also be used to elucidate the complex structure of these molecules and to further characterize their association with known inhibitors in order to rationally design new inhibitory herbicides. Alternatively, the recombinant protein can be used to isolate antibodies or peptides that modulate the activity and are useful in transgenic solutions.

IV. In vitro Inhibitor Assay: Discovery of Small Molecule Ligands That Interact with Essential Proteins Of Unknown Biochemical Function

Once a protein has been identified as a potential herbicide target based on its essentiality for normal plant growth and viability, a next step is to develop an assay that allows screening large number of chemicals to determine which ones interact with the protein. Although it is straightforward to develop assays for proteins of known function, developing assays with proteins of unknown functions can be more difficult.

To address this issue, novel technologies are used that can detect interactions between a protein and a compound without knowing the biological function of the protein. A short description of three methods is presented, including fluorescence correlation spectroscopy, surface-enhanced laser desorption/ionization, and biacore technologies.

Fluorescence Correlation Spectroscopy (FCS) theory was developed in 1972 but it is only in recent years that the technology to perform FCS became available (Madge et al. (1972) Phys. Rev. Lett., 29: 705-708; Maiti et al. (1997) Proc. Natl. Acad. Sci. USA, 94: 11753-11757). FCS measures the average diffusion rate of a fluorescent molecule within a small sample volume. The sample size can be as low as 10³ fluorescent molecules and the sample volume as low as the cytoplasm of a single bacterium. The diffusion rate is a function of the mass of the molecule and decreases as the mass increases. FCS can therefore be applied to protein-ligand interaction analysis by measuring the change in mass and therefore in diffusion rate of a molecule upon binding. In a typical experiment, the target to be analyzed is expressed as a recombinant protein with a sequence tag, such as a poly-histidine

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sequence, inserted at the N or C-terminus. The expression takes place in *E. coli*, yeast or insect cells. The protein is purified by chromatography. For example, the poly-histidine tag can be used to bind the expressed protein to a metal chelate column such as Ni2+ chelated on iminodiacetic acid agarose. The protein is then labeled with a fluorescent tag such as carboxytetramethylrhodamine or BODIPY® (Molecular Probes, Eugene, OR). The protein is then exposed in solution to the potential ligand, and its diffusion rate is determined by FCS using instrumentation available from Carl Zeiss, Inc. (Thornwood, NY). Ligand binding is determined by changes in the diffusion rate of the protein.

Surface-Enhanced Laser Desorption/Ionization (SELDI) was invented by Hutchens and Yip during the late 1980's (Hutchens and Yip (1993) Rapid Commun. Mass Spectrom. 7: 576-580). When coupled to a time-of-flight mass spectrometer (TOF), SELDI provides a mean to rapidly analyze molecules retained on a chip. It can be applied to ligand-protein interaction analysis by covalently binding the target protein on the chip and analyze by MS the small molecules that bind to this protein (Worrall et al. (1998) Anal. Biochem. 70: 750-756). In a typical experiment, the target to be analyzed is expressed as described for FCS. The purified protein is then used in the assay without further preparation. It is bound to the SELDI chip either by utilizing the poly-histidine tag or by other interaction such as ion exchange or hydrophobic interaction. The chip thus prepared is then exposed to the potential ligand via, for example, a delivery system capable to pipette the ligands in a sequential manner (autosampler). The chip is then submitted to washes of increasing stringency, for example a series of washes with buffer solutions containing an increasing ionic strength. After each wash, the bound material is analyzed by submitting the chip to SELDI-TOF. Ligands that specifically bind the target will be identified by the stringency of the wash needed to elute them.

Biacore relies on changes in the refractive index at the surface layer upon binding of a ligand to a protein immobilized on the layer. In this system, a collection of small ligands is injected sequentially in a 2-5 microlitre cell with the immobilized protein. Binding is detected by surface plasmon resonance (SPR) by recording laser light refracting from the surface. In general, the refractive index change for a given change of mass concentration at the surface layer, is practically the same for all proteins and peptides, allowing a single method to be applicable for any protein (Liedberg *et al.* (1983) Sensors Actuators 4: 299-304; Malmquist (1993) Nature, 361: 186-187). In a typical experiment, the target to be analyzed is expressed

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as described for FCS. The purified protein is then used in the assay without further preparation. It is bound to the Biacore chip either by utilizing the poly-histidine tag or by other interaction such as ion exchange or hydrophobic interaction. The chip thus prepared is then exposed to the potential ligand via the delivery system incorporated in the instruments sold by Biacore (Uppsala, Sweden) to pipette the ligands in a sequential manner (autosampler). The SPR signal on the chip is recorded and changes in the refractive index indicate an interaction between the immobilized target and the ligand. Analysis of the signal kinetics on rate and off rate allows the discrimination between non-specific and specific interaction.

Another assay for small molecule ligands that interact with a polypeptide is an inhibitor assay. For example, such an inhibitor assay useful for identifying inhibitors of the products of essential plant nucleic acid sequences, such as the essential *Arabidopsis* proteins described herein, comprises the steps of:

- a) reacting an essential Arabidopsis protein described herein and a substrate thereof in the presence of a suspected inhibitor of the protein's function;
- b) comparing the rate of enzymatic activity of the protein in the presence of the suspected inhibitor to the rate of enzymatic activity under the same conditions in the absence of the suspected inhibitor; and
- c) determining whether the suspected inhibitor inhibits the essential *Arabidopsis* 20 protein.

For example, the inhibitory effect on the activity of a hereindescribed essential Arabidopsis protein, may be determined by a reduction or complete inhibition of protein activity in the assay. Such a determination may be made by comparing, in the presence and absence of the candidate inhibitor, the amount of substrate used or intermediate or product made during the reaction.

V. Production of peptides

Phage particles displaying diverse peptide libraries permits rapid library construction, affinity selection, amplification and selection of ligands directed against an essential protein (H.B. Lowman, *Annu. Rev. Biophys. Biomol. Struct.* 26, 401-424 (1997)). Structural analysis of these selectants can provide new information about ligand-target molecule interactions and

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then in the process also provide a novel molecule that can enable the development of new herbicides based upon these peptides as leads.

VI. In Vivo Inhibitor Assay

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In one embodiment, a suspected herbicide, for example identified by *in vitro* screening, is applied to plants at various concentrations. The suspected herbicide is preferably sprayed on the plants. After application of the suspected herbicide, its effect on the plants, for example death or suppression of growth is recorded.

In another embodiment, an *in vivo* screening assay for inhibitors of the activity of a hereindescribed essential protein uses transgenic plants, plant tissue, plant seeds or plant cells capable of overexpressing a nucleotide sequence disclosed herein that encodes an essential protein, wherein the essential protein is enzymatically active in the transgenic plants, plant tissue, plant seeds or plant cells. A chemical is then applied to the transgenic plants, plant tissue, plant seeds or plant cells and to the isogenic non-transgenic plants, plant tissue, plant seeds or plant cells, and the growth or viability of the transgenic and non-transformed plants, plant tissue, plant seeds or plant cells are determined after application of the chemical and compared. Compounds capable of inhibiting the growth of the non-transgenic plants, but not affecting the growth of the transgenic plants are selected as specific inhibitors of the essential protein's activity.

The invention will be further described by reference to the following detailed examples. These examples are provided for purposes of illustration only, and are not intended to be limiting unless otherwise specified.

EXAMPLES

Standard recombinant DNA and molecular cloning techniques used here are well known in the art and are described by J. Sambrook, et al., Molecular Cloning: A Laboratory Manual, 3d Ed., Cold Spring Harbor, NY: Cold Spring Harbor Laboratory Press (2001); by T.J. Silhavy, M.L. Berman, and L.W. Enquist, Experiments with Gene Fusions, Cold Spring Harbor Laboratory, Cold Spring Harbor, NY (1984) and by Ausubel, F.M. et al., Current Protocols in Molecular Biology, New York, John Wiley and Sons Inc., (1988), Reiter, et al., Methods in Arabidopsis Research, World Scientific Press (1992), and Schultz et al., Plant Molecular Biology Manual, Kluwer Academic Publishers (1998). These references describe

the standard techniques used for all steps in tagging and cloning genes from *AclDs* transposon or T-DNA mutagenized populations of *Arabidopsis*: plant infection and transformation; screening for the identification of seedling mutants; and cosegregation analysis. *Ds* transposon insertion lines produced as described in Sundaresan *et al.* (1995) Genes and Dev., 9:1797-1810) are used in these experiments. T-DNA lines are generated using vacuum infiltration or floral dip methods (Bechtold *et al.* (1993) C. R. Acad. Sci. Paris, 316:1194-1199; Clough and Bent (1998) Plant J., 16:735-743; Desfeux *et al.* (2000) Plant Physiol., 123:895-904).

10 Example 1: Identification of Arabidopsis Mutants with Lethal Phenotypes

Essential genes are identified through the isolation of lethal mutants blocked in early development. Examples of lethal mutants include those blocked in the formation of the male or female gametes, embryo, or resulting seedling. Gametophytic mutants are found by examining insertion lines for the presence of 50% aborted pollen grains or ovules. Embryo defective lethal mutants usually produce 25% defective seeds following self-pollination of plants heterozygous for an insertion (see Errampalli *et al.* 1991, Plant Cell 3:149-157; Castle *et al.* 1993, Mol Gen Genet 241:504-514). Seedling lethal mutants usually segregate 25% seedlings that exhibit a lethal phenotype.

Example 2: Cosegregation Analysis for Lines with Lethal Phenotypes

The linkage of the mutation to the *Ds* or T-DNA insertion is established after identifying a transformed line segregating for a lethal phenotype of interest. A line segregating with a single functional insert will segregate for resistance in the ratio of about 2:1 (resistant: sensitive) to the selectable marker. In the case of an embryo defective mutant, one-quarter of the progeny of a plant heterozygous for an insertion will fail to germinate due to embryo lethality, resulting in a reduction of the normal 3:1 ratio to 2:1. In the case of a seedling lethal mutant, the seedlings with a mutant phenotype are excluded in the calculation of this ratio. Each of the resistant progeny is therefore heterozygous for the mutation if the *Ds* or T-DNA insertion is causing the mutant phenotype. To establish cosegregation of the insertion and the mutant phenotype, about 30 resistant progeny are transplanted to soil and each plant is shown to segregate the 25% progeny with a lethal phenotype by the appropriate screening of embryo or seedlings. When all resistant plants segregate the lethal phenotype,

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there is cosegregation of the insertion and the lethal mutation and the line is designated as "tagged."

Example 3: T-DNA Border Isolation by Plasmid Rescue

The plasmid rescue technique is used to molecularly clone Arabidopsis flanking DNA from one or both sides of the T-DNA insertion(s). Arabidopsis genomic DNA is isolated as described by Reiter et al. in Methods in Arabidopsis Research, World Scientific Press (1992). Genomic DNA is digested with a restriction endonuclease and ligated overnight. After ligation, the DNA is transformed into competent E. coli strain XL-1 Blue, DH10B, DH5 alpha, or the like, and colonies are selected on semi-solid medium containing ampicillin. Resistant colonies are picked into liquid medium with ampicillin and grown overnight. Plasmid DNA is isolated and digested with the rescue enzyme and analyzed on agarose gels containing ethidium bromide for visualization. Plasmids that represent different size classes are sequenced using primers that flank the plant DNA portion of the rescue element and the sequence is analyzed to determine what portion is plant DNA and what gene has been disrupted. The plasmid rescue is validated via PCR of template genomic DNA from a heterozygote for the insertion mutation. The experiment uses a primer anchored in the predicted flanking sequence and a primer in the T-DNA insertion. Finding a PCR product of the appropriate size, based on the sequence of the plasmid rescue clone confirms a valid rescue. Alternatively, Southern blot analysis with a probe that detects the relevant region of Arabidopsis DNA in genomic DNA from a heterozygote for the insertion mutation can be used to confirm the plasmid rescue results.

Example 4: Transposon or T-DNA Border Isolation by TAIL-PCR

Arabidopsis genomic DNA is isolated according to Reiter et al. in Methods in Arabidopsis Research, World Scientific Press (1992) or using the Nucleon PhytoPure™ Plant DNA isolation kit (Amersham International plc, Buckinghamshire, England) or the Puregene DNA isolation kit (Gentra Systems, Minneapolis, MN). Fragments of genomic DNA flanking the borders of the transposon or T-DNA are isolated using the TAIL-PCR technique (Liu et al. (1995) Plant J., 8:457-463; Liu and Whittier (1995), Genomics, 25:674-681). Three sets of 12 TAIL-PCR reactions, referred to as the primary, secondary and tertiary reactions, are performed. In each reaction, one arbitrary degenerate primer and one transposon-specific or

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T-DNA-specific primer are used. The arbitrary degenerate primer is chosen from among seven primers, LWAD1, CA50, CA51, CA52, CA53, CA54, and CA55 (Table 1), which are used to prime the genomic DNA flanking the insertion. Alternatively, less than 12 TAIL-PCR reactions are done using fewer arbitrary degenerate primers. These degenerate primers are used in combination with two sets of three, nested, transposon-specific primers (Table 2) or T-DNA-specific primers (Table 3). The transposon-specific primers are homologous to regions of the Ds elements that lie at the outermost ends of the transposons, DS5 at the 5' end (primers 5A, 5B, and 5C) and DS3 at the 3' end (primers 3A, 3B, and 3C). The T-DNAspecific primers are homologous to regions of the T-DNA that lie in the borders of the T-DNAs. For the pCSA104 and pDAP101 T-DNAs, right borders are recovered with CA66 10 (primary primer), CA67 (secondary primer), and CA68 (tertiary primer) and left borders are recovered with JM33 (tertiary primer); JM34 (secondary primer); and JM35 (primary primer). For the pCSA110 T-DNA, right borders are recovered with QRB1 (primary primer), QRB2 (secondary primer), and QRB3 (tertiary primer) and left borders are recovered with JM33 (tertiary primer); JM34 (secondary primer); and JM35 (primary primer). For the 15 pPCVICEn4HPT (Hayashi et al. (1992), Science, 258:1350-1353) and pSKI015 (Weigel et al. (2000) Plant Physiol. 122:1003-1014) T-DNAs, left borders are recovered with SKI1 (primary primer), SKI2 (secondary primer), and SKI3 (tertiary primer). When the degenerate and nested primer pairs are used in a series of low and high-stringency PCR amplifications, as described in the TAIL-PCR protocol (Liu and Whittier (1995), Genomics, 25:674-681), DNA 20 fragments are produced that correspond to the genomic DNA that is directly adjacent to the transposon or T-DNA insertion. The nucleic acid sequences of the PCR products from the tertiary TAIL-PCR reactions are then determined by standard molecular biology techniques. The resulting sequences are analyzed for the presence of non-Ds transposon or non-T-DNA 25 vector sequence.

To confirm the integrity of the resultant products, PCR primers specific to the flanking genomic region are designed and used in conjunction with the tertiary nested primer in a PCR reaction, to confirm the transposon or T-DNA insertion point within the genomic DNA. Finding a PCR product of the appropriate size, based on the sequence of the TAIL-PCR clone confirms a valid rescue.

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Table 1: Arbitrary Degenerate Primers

	SEQ ID NO:	<u>Primer</u>	Degen.	Primer Sequence
	101	LWAD1	1026	ngt tgw gna twt sgw gnt
	102	CA50	128	ngt cga swg ana wga a
5	103	CA51	128	tgw gna gsa nca sag a
	104	CA52	128	agw gna gwa nca wag g
	105	CA53	256	stt gnt ast nct ntg c
	106	CA54	64	ntc gas twt sgw gtt
	107	CA55	256	wgt gna gwa nca nag a

Table 2: Nested Primers For Ds Lines

	SEQ ID NO:	<u>Primer</u>	Primer Sequence
	108	5A	actagetetacegttteegttteegtttac
	109	5B	ttacctcgggttcgaaatcgatcgggataa
15	110	5C	aaaatcggttatacgataacggtcggtacggga
	111	3A	gggtcttgcggatctgaatatatgttttcatgtgtg
	112	3B	taccgaagaaaaataccggttcccgtccgatttcgac
	113	3C	ggatcgtatcggttttcgattaccgtatttatcc

20 Table 3: Nested Primers For T-DNA Lines

	SEQ ID NO:	<u>Primer</u>	Primer Sequence
	114	CA66	att agg cac ccc agg ctt tac act tta tg
	115	CA67	gta tgt tgt gtg gaa ttg tga gcg gat aac
	116	CA68	taa caa ttt cac aca gga aac agc tat gac
25	117	JM33	tag cat ctg aat ttc ata acc aat ctc gat aca c
	118	JM34	get tee tat tat ate tte eea aat tae eaa tae a
	119	JM35	gcc ttt tca gaa atg gat aaa tag cct tgc ttc c
	120	QRB1	caa act agg ata aat tat cgc gcg cgg tgt ca
	121	QRB2	ggt gtc atc tat gtt act aga tcg gga att ga
30	122	QRB3	cgc cat ggc ata tgc tag cat gca taa ttc
	123	SKI1	aat tgg taa tta ctc ttt ctt ttc ctc cat att ga
	124	SKI2	ata ttg acc atc ata ctc att gct gat cca t
	125	SKI3	tga tcc atg tag att tcc cgg aca tga a

Example 5: Transposon or T-DNA Border Isolation by TAIL2k PCR

Arabidopsis genomic DNA is isolated according to Reiter et al. in Methods in Arabidopsis Research, World Scientific Press (1992) or using the Nucleon PhytoPure™ Plant DNA isolation kit (Amersham International plc, Buckinghamshire, England) or the Puregene DNA isolation kit (Gentra Systems, Minneapolis, MN). Fragments of genomic DNA flanking the borders of the transposon or T-DNA are isolated using the TAIL2k PCR technique. Two sets of 12 TAIL-PCR reactions, referred to as the primary and secondary reactions, are performed. In each reaction, one arbitrary degenerate primer and one transposon-specific or T-DNA-specific primer are used. The arbitrary degenerate primer is selected from among six primers; CA50, CA51, CA52, CA53, CA54, and CA55 (Table 1), which are used to prime the genomic DNA flanking the insertion. Alternatively, less than 12 TAIL-PCR reactions are done using fewer arbitrary degenerate primers. These degenerate primers are used in combination with two sets of two, nested, transposon-specific primers (Table 2) or T-DNAspecific primers (Table 3). The transposon-specific primers are homologous to regions of the Ds elements that lie at the outermost ends of the transposons, DS5 at the 5' end (primers 5A, 5B, and 5C) and DS3 at the 3' end (primers 3A, 3B, and 3C). The T-DNA-specific primers are homologous to regions of the T-DNA that lie in the borders of the T-DNAs. For the pCSA104 and pDAP101 T-DNAs, right borders are recovered with CA66 (primary primer), CA67 (secondary primer), and CA68 (sequencing primer) and left borders are recovered with JM33 (sequencing primer), JM34 (secondary primer), and JM35 (primary primer). Primers CA66, CA67, and CA68 are also known as RB1, RB2, and RB3, respectively. Primers JM35, JM34, and JM33 are also known as LB1, LB2, and LB3, respectively. For the pCSA110 T-DNA, right borders are recovered with QRB1 (primary primer), QRB2 (secondary primer), and ORB3 (sequencing primer) and left borders are recovered with JM33 (sequencing primer); JM34 (secondary primer); and JM35 (primary primer). For the pPCVICEn4HPT (Hayashi et al. (1992), Science, 258:1350-1353) and pSKI015 (Weigel et al. (2000) Plant Physiol. 122:1003-1014) T-DNAs, left borders are recovered with SKI1 (primary primer), SKI2 (secondary primer), and SKI3 (sequencing primer). When the degenerate and nested primer pairs are used in a series of low and high-stringency PCR amplifications, as described in the TAIL-PCR protocol (Liu and Whittier (1995), Genomics, 25:674-681), DNA fragments are produced that correspond to the genomic DNA that is directly adjacent to the transposon

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or T-DNA insertion. TAIL2k-PCR differs from the original TAIL-PCR protocol by the elimination of the tertiary PCR and modification of the secondary PCR. The cycling conditions used in the secondary reaction are modified to include 5 high annealing temperature cycles (64 degrees C) at the beginning, three additional so-called super cycles, and five additional low annealing temperature cycles (44 degrees C) at the end of the reaction. The melting and extension times are the same as all other TAIL-PCR reactions. Additionally, the reaction volume is increased to 40 microliters. The nucleic acid sequences of the PCR products from the secondary TAIL2k-PCR reactions are then determined by standard molecular biology techniques. The resulting sequences are analyzed for the presence of non-Ds transposon or non-T-DNA vector sequence.

To confirm the integrity of the resultant products, PCR primers specific to the flanking genomic region are designed and used in conjunction with the tertiary nested primer in a PCR reaction, to confirm the transposon or T-DNA insertion point within the genomic DNA. Finding a PCR product of the appropriate size, based on the sequence of the TAIL2k-PCR sequencing result confirms a valid rescue.

Example 6: Identification of Both Borders of a T-DNA or Ds Insertion

If the results of border rescue provide information on only one of the two borders for an insertion in a given line, additional experiments are performed to identify the second border. These experiments are necessary to show that a single gene has been disrupted in a given line. In some cases, an insertion can affect more than a single gene due to a chromosomal deletion or rearrangement. In those cases, additional experiments are required to identify which of the affected genes is responsible for the lethal phenotype.

When both borders of an insertion are not recovered, primers are designed to isolate a PCR product that will provide information on the location of the missing border. Three primers are chosen in *Arabidopsis* genomic DNA on the opposite side of the insertion about one, two, and five kb away from the insertion point; the primers point towards the expected second border. Long PCR conditions (Advantage 2, Clontech) are then employed following the manufacturer's directions to amplify the relevant region from genomic DNA isolated from a heterozygote for the lethal mutation. PCR reactions are performed using appropriate pairs of genomic and T-DNA or *Ds* border primers. Finding a PCR product of the appropriate size,

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based on the sequence of the TAIL-PCR clone confirms a valid rescue of the second border. In some cases, the PCR product is directly sequenced to determine the exact insertion point.

If the second border is not recovered with this method, an additional set of PCR reactions are preformed. In these experiments, the genomic primers are paired with a series of internal T-DNA or Ds primers designed at about one kb intervals in both orientations across the entire T-DNA or Ds vector sequence. Finding a PCR product of the appropriate size, based on the sequence of the TAIL-PCR clone confirms a valid rescue of the second border. In some cases, the PCR product is directly sequenced to determine the exact insertion point. Any borders recovered with this approach are classified as abnormal because they lack the ends of the Ds transposon or the expected 24 bp T-DNA imperfect repeat characteristic of right and left borders.

Example 7: Identification of Insertion Points for Lines with Lethal Phenotypes

For each line with a lethal phenotype, the sequences of the borders of the insertion are determined and the insertion points in the *Arabidopsis* genome are deduced. For *Ds* insertion lines, PCR products are obtained from the Ds3 and Ds5 borders. For T-DNA lines, PCR products or plasmid rescue clones are obtained from left (LB), right (RB), or abnormal (AB) borders. These sequences are used in BLASTn searches against nucleotide databases (Altschul *et al.* (1990) J Mol. Biol. 215:403-410; Altschul *et al.* (1997) Nucleic Acids Res. 25:3389-3402). The results are summarized in Table 4. *Ds* line names begin with ET or GT; T-DNA line names are numbers. The insertion point (Insert Pt.) and the direction of the flanking sequence (Dir.) either up (U) or down (D) in the genome section is noted. Often, small deletions or duplications of genomic DNA accompany the insertion of a T-DNA or *Ds* transposon.

The gene that has been inactivated in a given line with a lethal phenotype is determined from the insertion points for that line. Often, the precise location of an ORF for a given gene is not known, but predictions are available in genome sections deposited in GenBank. The precise boundaries of that ORF is determined as described in Example 7.

Table 4: Insertion Points For Lines With Lethal Phenotypes

Gene	Line#	Border	Genome Section	Acc. #	Insert Pt.	Dir.
942	942	LB	K24G6	AB012242	33667	D

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770	978	LB	F23N20	AC016972	58221	D
978	978 978	LB	F23N20	AC016972	58301	U
010	3218	LB	T8K14	AC007202	10500	D
218	3218	LB	T8K14	AC007202	10540	U
15.62	4563	LB	ATCHRII092	AC006438	25542	D
1563	8794	LB	F2J6	AC009526	45854	D
3794	8794 8794	LB	F2J6	AC009526	45879	U
2106	9106	LB	T2J13	AL132967	78013	U
9106	9106	AB	T2J13	AL132967	77943	D
10708	10708	RB	F1I21	AC005687	40005	D
10708	10708	LB	F1I21	AC005687	40042	U
	70241	LB	F1I21	AC005687	40210	D
	70241	RB	F1I21	AC005687	40215	U
10044	10844	LB	F13F21	AC007504	60873	U
10844	10844	LB	F13F21	AC007504	60839	D
10051	10951	LB	MKP11	AB005238	20298	D
10951	10951	LB	MKP11	AB005238	20318	U
12935	12935	LB	ATCHRII150	AC005168	36510	D
12933	12935	LB	ATCHRII150	AC005168	36545	U
13823	11361	LB	T27G7	AC006932	78096	U
13623	11361	AB	T27G7	AC006932	78065	D
	13823	LB	T27G7	AC006932	78096	U
	13823	RB	T27G7	AC006932	77722	D
14519	14519	LB	ATCHRIV72	AL161576	50259	U
14317	14519	AB	ATCHRIV72	AL161576	50228	D
14610.1	14610.1	LB	F4P13	AC009325	55319	U
14010.1	14610.1	RB	F4P13	AC009325	55442	D
14891	14891	LB	ATCHRIV89	AL161593	11412	U
1-1057	14891	RB	ATCHRIV89	AL161593	11313	D
14986	14986	LB	K10D20	AP000410	51816	D
14,500	14986	RB	K10D20	AP000410	54505	U
15377	15377	RB	F28G11	AC074025	19572	D
100,,	15377	LB	F28G11	AC074025	19587	U
16219	16219	LB	MRO11	AB005244	51998	<u>U</u>
1021	16219	LB	MRO11	AB005244	51995	<u>D</u>
16547	16547	LB	ATCHRIV65	AL161565	80692	D
700	16547	RB	ATCHRIV65	AL161565	80791	<u>U</u>
20933	20933	LB	ATCHRII146	AC004747	47678	D
20,55	20933	LB	ATCHRII146	AC004747	47683	U
21455	21455	LB	ATCHRIV54	AL161554	105596	U
21.55	21455	RB	ATCHRIV54	AL161554	105542	<u>D</u>
21878	21878	LB	T19F11	AC009918	19609	<u>_</u>
23915	23915	LB	ATCHRII008	AC005936	49629	<u>T</u>
23713	23915	LB	ATCHRII008	AC005936	49657	<u>U</u>
30945	30945	LB	ATCHRII192	AC004238	2411	1
30773	30945	LB	ATCHRII192	AC004238	2410	Ţ

21005	21905	LB	MTI20	AB013396	52020	D
31895	31895	LB	MTI20	AB013396	52089	U
24260	31895	LB LB	T4O12	AC007396	92811	_ <u>U</u>
34269	34269	RB	T4012	AC007396	92808	D
24540	34269 34540	LB	T1G11	AC002376	41572	D
34540				AC002376	41608	-
	34540	<u>LB</u>	TIG11	AC002376 AC002376	41494	U
	72902	LB	T1G11	AC002376 AC002376	41465	D
01555	72902	LB	T1G11	AC002370 AC004393	42152	D
34555	34555	LB	T1F15			- 6
	54334	RB	T1F15	AC004393	41803	
	54334	<u>LB</u>	T1F15	AC004393	41671	D
35154	35154	RB_	MWD9	AB007651	45718	D
	35154	LB	MWD9	AB007651	45732	U
35438	35438	LB	MAL21	AP000383	25170	D
	35438	<u>LB</u>	MAL21	AP000383	25738	U
37351	37351	LB	F25C20	AC007296	52890	U
	37351	RB	F25C20	AC007296	52196	D
37389	37389	LB	F3F19	AC007357	45488	U
	37389	RB	F3F19	AC007357	45471	D
38108	38108	LB_	ATCHRII150	AC005168	83430	D
	38108	RB	ATCHRII150	AC005168	83446	U
43301	43301	RB	T22D16	AL357612	57549	D
	43301	LB	T22D16	AL357612	57599	U
46250	46250	LB	F17A9	AC016827	74222	D
	46250	RB	F17A9	AC016827	74274	U
47050A	47050	LB	T23E18	AC009978	49445	D
	47050	RB	T23E18	AC009978	49475	U
52949A	52949	LB	K16H17	AB016884	34713	D
	52949	LB	K16H17	AB016884	34718	U
53210A	53210	RB	ATCHRII017	AC007167	92796	D
	53210	LB	ATCHRII017	AC007167	92942	U
	69121	LB	ATCHRII017	AC007167	94478	D
	69121	LB	ATCHRII017	AC007167	94502	U
55483	55483	RB	ATCHRII164	AC005727	71269	U
	55483	LB	ATCHRII164	AC005727	71258	D
58351A	58351	RB	МҮН9	AB016893	42547	D
	58351	LB	МҮН9	AB016893	42772	U
60944	60944	LB	F1B16	AC023754	89492	Ū
	60944	LB	F1B16	AC023754	89428	D
62837	62837	LB	T21J18	AL132963	70906	U
	62837	LB	T21J18	AL132963	70873	D
65310	65310	LB	T20H2	AC022472	8158	U
	65310	RB	T20H2	AC022472	8096	D
68181	68181	RB	F12A12	AL133314	38270	U
00101	68181	LB	F12A12	AL133314	38275	D
70913	70913		1 14/114	AL353013	5347	$\overline{\overline{\mathbf{D}}}$

	70913	LB	T24H18	AL353013	5358	U
71067	71067	LB	F2E2	AC069252	63031	U
71007	71067	LB	F2E2	AC069252	62932	D
71654	71654	RB	MYA6	AB023046	71956	U
71054	71654	LB	MYA6	AB023046	71907	D
ET3172	ET3172	DS5	ATCHRIV4	AL161492	134442	<u>U</u>
ET3546	ET3546	DS3	ATCHRII115	AC006081	20874	<u>D</u>
D13340	ET3546	DS5	ATCHRII115	AC006081	20973	<u>U</u>

Example 8: Identification of cDNAs for Essential Genes

A cDNA for a gene identified as essential is identified using a variety of approaches. This information enables the ORF for a given gene to be identified and used for other experiments including expression of the corresponding protein in heterologous systems.

If there is a full-length cDNA deposited in GenBank or published elsewhere, that sequence may be checked independently using methods described below. Alternatively, the sequence may be considered to be correct.

In some cases, there are published EST sequences that can be assembled to cover the entire ORF from start codon to stop codon. This sequence may be checked independently using methods described below or it may be considered to be correct.

Often part of the cDNA is published and this information can be used to identify the entire ORF. If the 5' end containing the start codon is known, 3' RACE is performed to identify the remainder of the cDNA. If the 3' end containing the stop codon is known, 5' RACE is performed to identify the remainder of the cDNA. If both the 5' and the 3' ends are known, but the sequence between the two ends of the cDNA is not known, PCR is performed with primers hybridizing to each end of the cDNA. In all three of these cases, PCR is performed using template DNA from a GeneRacer (Invitrogen) or a Marathon (Clontech) cDNA library prepared from RNA isolated from seedling tissue. A resulting PCR product is TA-cloned (Original TA-Cloning kit, Invitrogen) and sequenced.

If no part of the cDNA is published, the cDNA is identified by starting from gene model predictions in the annotation for genomic clones or elsewhere. To identify the ORF, primers are designed to the 5' and 3' ends of the predicted ORF. PCR is performed using template DNA from a cDNA library prepared from seedling tissue or the pFL61 Arabidopsis cDNA library (Minet et al. (1992) Plant J. 2: 417-422). The resulting PCR product is TAcloned (Original TA-Cloning kit, Invitrogen) and sequenced. Alternatively, 5' and 3' RACE are performed with primers predicted by gene models to be in exons. PCR is performed using

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template DNA from a GeneRacer (Invitrogen) or a Marathon (Clontech) cDNA library prepared from RNA isolated from seedling tissue. A resulting PCR product is TA-cloned (Original TA-Cloning kit, Invitrogen) and sequenced.

If the cDNA sequence is the same as the sequence predicted in the GenBank annotation, the experiments confirm for the first time the actual ORF. If the cDNA sequence is not the same as the sequence predicted in the GenBank annotation, the experiments identify for the first time the actual ORF. In some cases, more than one cDNA sequence is found for a given gene and both sequences are included in this application.

10 Example 9: Description of Essential Genes

The putative function of the protein encoded by each essential gene is determined from analysis of the ORF in each cDNA. Information from the relevant *Arabidopsis* genomic section deposited in GenBank is used as a starting point to explore the function of a given gene. This analysis also includes BLAST searches (Altschul *et al.* (1990) J. Mol. Biol. 215:403-410; Altschul *et al.* (1997) Nucleic Acids Res. 25:3389-3402) of sequence databases to identify similar proteins. Table 5 describes the putative functions for the essential genes discovered in this application.

Table 5: Putative Functions For Essential Genes

Gene	SEQ ID Nos:	Putative Function & Similar Genes	References
00942	1-2	similarity to disease resistance protein large gene family in Arabidopsis including disease resistance proteins RPP1-WsA,B&C similar to tobacco TMV resistance protein N	Whitham, S. et al. (1994) Cell 78:1101-1115; Botella, M.A., et al. (1998) Plant Cell 10: 1847-1860
00978	3-4	unknown protein similar to Arabidopsis protein of unknown function (CAB87660) & ESTs from many plants	none
03218	5-6	AAA ATPase similar to <i>E. coli</i> FtsH cell division protein (P28691) that acts as an ATP-dependent metallopeptidase; homologs in many species	Schumann, W. (1999) FEMS Microbiol Rev 23:1-11; Langer, T. (2000) Trends Biochem Sci 2000 25:247-251

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04563	7-8	unknown protein large gene family in Arabidopsis of unknown function proteins	none
08794	9-10	putative histidine decarboxylase similar to Brassica, tomato (tom92), and rice putative histidine decarboxylases	Picton, S et al. (1993) Plant Mol Biol 23:627-631; Watanabe, T et al. (1990) Trends Pharmacol Sci 11:363- 367; Vaaler, G.L. & Snell, E.E. (1989) Biochemistry 28:7306-7313
09106	11-12	cytosolic 40S ribosomal protein S11-alpha	Browning, K.S. (1996) <i>Plant Mol Biol</i> 32:107-144; Gantt, J. S. & Thompson, M.D. (1990) <i>J. Biol Chem</i> 265:2763-2767
10708	13-14	cytoplasmic 60S ribosomal protein L3	Peltz, S.W. et al. (1999) Mol Cell Biol 19:384-391; Kim, Y. et al. (1990) Gene 93:177- 182; Wickner, R.B et al. (1982) Proc Natl Acad Sci USA 79:4706-4708
10844	15-16	40S ribosomal protein S17-like	Gantt, J.S. & Thompson, M.D. (1990) <i>J Biol Chem</i> 265:2763-2767; Wiener, L. et al. (1988) <i>Nucleic Acids Res</i> 16:1233-1250
10951	17-18	phytoene synthase	Welsch, R. et al. (2000) Planta 211:846-854; Shewmaker, C.K. et al. (1999) Plant J. 20:401-412; Von Lintig, J. et al. (1997) Plant J. 12:625-634
12935	19-20	putative choline kinase similar to soybean choline kinase (T08815) and mouse & human choline/ethanolamine kinases	Monks, D.E. et al. (1996) Plant Physiol. 110:1197-1205; Bligny, R. et al. (1989) J Biol Chem. 264:4888-4895; Wharfe, J. & Harwood, J.L. (1979) Biochim Biophys Acta. 575:102-111
13823	21-22	magnesium protoporphyrin IX chelatase subunit D	Papenbrock, J. et al. (1997) Plant J. 12:981-990; Papenbrock, J. et al. (2000) Plant Physiol. 122:1161-1169; Luo, M. et al. (1999) Plant Mol Biol. 41:721-731; Jensen, P.E. et al. (1996) Mol. Gen. Genet. 250:383-394

14519	23-24	putative protein small gene family in Arabidopsis of unknown function proteins	none
14610.1	25-26	putative cell division control protein; similar to cdc48, AAA ATPase proteins similar to S. pombe AAA ATPase (CAB16902); Arabidopsis cdc48 homolog (P54609); cdc48/valosin-containing protein homologs from soybean, Capsicum annuum, rice, Dictylostelium; Drosophila smallminded	Frohlich, K.U. et al. (1991) J Cell Biol. 114:443-453; Feiler, H.S. et al. (1995) EMBO J. 14:5626-5637; Langer, T. (2000) Trends Biochem Sci 2000 25:247-251
14891	27-28	putative protein contains PFAM 02536 mTERF (mitochondrial transcription termination factor) domain; large gene family in Arabidopsis of unknown function proteins	Fernandez-Silva, P. et al. (1997) EMBO J 16:1066-1079
14986	29-30	ubiquitin isopeptidase T (aka ubiquitin-specific protease 14)	Wilkinson, K.D. et al. (1995) Biochemistry 34:14535- 14546; Falquet, L. et al. (1995) FEBS Lett 376:233- 237; Lindsey, D.F. et al. (1998) J Biol Chem 273:29178-29187
15377	31-32	putative formyl transferase similar to <i>B. napus</i> methionyl tRNA transformylase Fmt protein (AJ245479) & <i>B. rapa</i> S-locus protein 8 (AB022076)	Cui Y et al. (1999) Plant Cell. 11:2217-2231; Suzuki, G. et al. (1999) Genetics 153:391- 400; Cusack S. (1999) Curr Opin Struct Biol. 9:66-73
16219	33-34	polyadenylation cleavage/specificity factor 100 kDa subunit (AF283277)	Bilger, A. et al. (1994) Genes Dev. 8:1106-1116; Bienroth, S. et al. (1993) EMBO J. 12:585-594; Jenny, A. et al. (1994) Mol Cell Biol. 14:8183-8190
16547	35-36	similarity to UV-induced protein Uvi31, S. pombe, G1381578 unknown function, but similar to Pectobacterium chrysanthemi SufE protein (AJ301654) involved in iron metabolism, S. pombe uvi31 protein of the BolA / YRBA family (Q12238), Synechocystis hypothetical 17.7 KDA protein SLR1419 (P74523)	Kim, S.H. et al. (1997) Environ Mol Mutagen 30:72-81; Santos, J.M. et al. (1999) Mol Microbiol 32:789-798

			NT T I -4 -1 (1004) Notice
20933	37-38	hypothetical protein	Neer, E.J. et al. (1994) Nature
		contains WD40 repeats, similar to	371:297-300; Johnstone, R.W.
j		human CIAO 1 gene (O76071) &	et al. (1998) J Biol Chem
		S. cerevisiae YDR267c (S70127)	273:10880-10887
21455	39-40	putative protein	none
		small gene family in Arabidopsis	•
		of unknown function proteins	
21878	41-42	Arabidopsis	Dormann, P. et al. (1999)
		digalactosyldiacylglycerol	Science 284:2181-2184;
		synthase (DGD1, AAD42378)	Hartel, H. et al. (1997) Plant
			Physiol 115:1175-1184
23915	43-44	hypothetical protein	Small, I.D. & Peeters, N.
23313		contains PPR motifs, member of	(2000) Trends Biochem Sci
		large gene family in Arabidopsis	25:46-47; Manthey, G.M. &
		large gene lanning in Theorem parts	McEwen, J.E. (1995) <i>EMBO J</i>
			14:4031-4043; Barkan, A. et
			al. (1994) EMBO J 13:3170-
			3181
30945	45-46	unknown protein	none
30943	43-40	similar to rice hypothetical protein	Hone
		(BAB56056)	
21005	47-48	similar to unknown protein	none
31895	47-48		none
		small gene family in Arabidopsis	
0.4060	10.50	of unknown function proteins	none
34269	49-50	unknown protein	Reed, K.E. & Cronan, J.E. Jr.
34540	51-52	probable lipoate protein ligase B,	(1993) J Bacteriol 175:1325-
		similar to Mycobacterium LIPB	1336; Chen, X.J. (1997) Mol.
		gene (O32961)	Gen. Genet. 255:341-349
		also similar to S. pombe putative	Gen. Genet. 255.541-549
		pre-tRNA/pre-rRNA processing	
		protein (T41635)	
34555	53-54	similar to Synechocystis	none
		hypothetical 41.9KD protein	
		(P52640)	
		similar to several prokaryotic	
		proteins of unknown function	
		including E. coli YJEQ (P39286)	
35154	55-56	similar to unknown protein	Shpakovskii, G.V. &
		similar to human hypothetical	Lebedenko, E.N. (1997)
		protein (BAA91556), S. cerevisiae	Bioorg. Khim. 23:234-237
1		probable membrane protein	1
		YOR262w (S67159), & S. pombe	
		ATP(GTP)-binding protein Fet5	
		(AAC49837)	
35438	57-58	unknown protein	none
		weak similarity to Pennisetum	
		ciliare unknown function protein	
		(AAK15504)	
i	1	(AAK1JJU4)	

37351	59-60	strong similarity to obtusifoliol 14- alpha demethylase (CYP51; P93846) from Sorghum bicolor (also wheat & rice), member of the PFI00067 cytochrome P450 family	Kushiro, M. et al. (2001) Biochem Biophys Res Commun. 285:98-104; Bak et al. (1997) Plant J. 11:191-201; Grausem, B. (1995) Plant J. 7:761-770
37389	61-62	similar to human GLE1-like required for poly(A)+ RNA export (AAC25561)	Watkins, J.L. et al. (1998) Proc. Natl. Acad. Sci. U.S.A. 95:6779-6784; Murphy, R. & Wente, S.R. (1996) Nature 383:357-360
38108	63-64	Arabidopsis 4-(cytidine 5'- phospho)-2-C-methyl-D-erythritol kinase (aka ispE & 4- diphosphocytidyl-2-C-methyl- Derythritol kinase) (AF288615) similar to E. coli ychB (aka ispE) gene (P24209)	Rohdich, F. et al. (2000) Proc Natl Acad Sci U.S.A. 97:8251-8256; Luettgen, H. et al. (2000) Proc. Natl. Acad. Sci. U.S.A. 97:1062-1067; Lange, B.M. & Croteau, R. (1999) Proc Natl Acad Sci U.S.A. 96:13714-13719
43301	65-66	similar to hypothetical bacterial proteins, including <i>Pseudomonas</i> aeruginosa protein PA0292 (F83608) & Lactococcus lactis (AAK05795)	none
46250	67-68	hypothetical protein weak similarity to hypothetical proteins from Arabidopsis (AAG51506) and mouse (BAB23375)	none
47050A	69-70	unknown protein weak similarity to Botrytis cDNA (AL115827)	none
52949A	71-72	6-phosphogluconolactonase-like protein similar to 6-phosphogluconolactonases such as human (O95336), Brassica carinata (AAK50346), & Mycobacterium tuberculosis (devB, CAB09261)	
53210A	73-74	putative heat shock protein in hsp90 family similar to rye hsp82 (S65776), Ipomoea nil hsp83 (P51819), chicken hsp90 beta (Q04619) and others	Felsheim, R.F. & Das, A. (1992) Plant Physiol. 100:1764-1771; Coates, A.R. et al. (1999) Biotechnol Genet Eng Rev 16:393-405; Milioni, D. & Hatzopoulos, P. (1997) Plant Mol Biol 35:955-961

55483 58351A	75-76	putative para-aminobenzoate synthase and glutamine amidotransferase, a bifunctional enzyme similar to Streptomyces pristinaespiralis papA (AAC44866), E. coli pabB (P05041) & pabA (P00903), and Bacillus stearothermophilus anthranilate synthase component I trpE (AAD33791) 26S proteasome p55 protein-like similar to human 26S proteasome	Goncharoff, P. & Nichols, B.P. (1984) J Bacteriol. 159:57-62.; Roux, B. & Walsh, C.T. (1992) Biochemistry. 31:6904-6910; Kaplan, J.B. & Nichols, B.P. (1983) J Mol Biol 168:451-468 Saito, A. et al. (1997) Gene 203:241-250; Glickman, M.H.
		regulatory complex chain p55 (BAA19749), S. cerevisiae 26S proteasome regulatory complex chain RPN5 (S67695), and others	et al. (1998) Mol Cell Biol 18:3149-3162
60944	79-80	similar to Guillardia theta chloroplast 50S ribosomal protein L31 (O46917)	Yamaguchi, K. & Subramanian, A.R. (2000) <i>J Biol Chem</i> , 275:28466-28482
62837	81-82	AtClpC: regulatory subunit of Clp protease with ATPase activity (BAA82062)	Adam, Z. (2000) Biochimie 82:647-654; Sokolenko, A. et al. (1998) Planta 207:286-295; Nakabayashi, K. et al. (1999) Plant Cell Physiol. 40:504- 514; Maurizi, M.R. et al. (1990) J Biol Chem. 265:12536-12545
65310	83-84	26S proteasome regulatory subunit S3, contains a PCI PFI01399 domain similar to 26S proteasome regulatory subunit S3 from Nicotiana tabacum (P93768), carrot (Q06364), human (O43242), S. cerevisiae RPN3 (P40016), and others	
68181	85-86	small zinc finger-like protein TIM9 similar to mitochondrial import inner membrane translocase subunit TIM9 from several plants and S. cerevisiae (O74700)	Koehler, C.M. et al. (1998) EMBO J. 17:6477-6486; Tokatlidis, K. et al. (2000) Biochem Soc Trans 28:495- 499
70913	87-88	Arabidopsis CCAAT binding protein/transcription factor Hap2a (CAA74048)	Edwards, D. et al. (1998) Plant Physiol 117:1015-1022; Albani, D. & Robert, L.S. (1995) Gene 167:209-213

71067	89-90	hypothetical protein gene family in <i>Arabidopsis</i> of unknown function proteins	none
71654	91-92	poly(A) binding protein-like	Hilson, P. et al. (1993) Plant Physiol 103:525-533; Belostotsky, D.A. & Meagher, R.B. (1993) Proc Natl Acad Sci U.S.A. 90:6686-6690; Gallie, D.R. (1998) Gene 216:1-11
ET3172	93-94	hypothetical protein small gene family in Arabidopsis (T47999 & T02193) of unknown function	none
ET3546	95-96	cdc27/nuc2-like protein, may contain TPR-repeat similar to human cdc27 (P30260), S. pombe nuc2 (P10505), S. cerevisiae cdc23 (P16522), and others	Hirano, T. et al. (1988) J. Cell Biol. 106:1171-1183; Chen, P.L. et al (1995) Cell Growth Differ. 6:199-210

Example 10: Expression of Recombinant Essential Proteins in E. coli

The coding region of each of the essential proteins, corresponding to cDNA clones of odd-numbered SEQ ID NO:1-96, is subcloned into an appropriate expression vector, and transformed into *E. coli* using the manufacturer's conditions. Specific examples include plasmids such as pBluescript (Stratagene, La Jolla, CA), pFLAG (International Biotechnologies, Inc., New Haven, CT), and pTrcHis (Invitrogen, La Jolla, CA). *E. coli* is cultured, and expression of the essential protein is confirmed. Recombinant protein is isolated using standard techniques.

Example 11: In Vitro Binding Assays

Recombinant protein for each of the essential genes described in this application is obtained, for example, according to Example 10. The protein is immobilized on chips appropriate for ligand binding assays using techniques that are well known in the art. The protein immobilized on the chip is exposed to sample compound in solution according to methods well know in the art. While the sample compound is in contact with the immobilized protein, measurements capable of detecting protein-ligand interactions are conducted. Examples of such measurements are SELDI, biacore and FCS, described above. Compounds

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found to bind the protein are readily discovered in this fashion and are subjected to further characterization.

The above-disclosed embodiments are illustrative. This disclosure of the invention will place one skilled in the art in possession of many variations of the invention. All such obvious and foreseeable variations are intended to be encompassed by the present invention.

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CLAIMS:

- 1. A method of identifying a herbicidal compound, comprising:
 - a) combining a polypeptide comprising an amino acid sequence at least 90% identical to an amino acid sequence selected from the group consisting of the even numbered SEQ ID NOs:2-96 with a compound to be tested for the ability to bind to said polypeptide, under conditions conducive to binding;
 - b) selecting a compound identified in (a) that binds to said polypeptide;
 - c) applying a compound selected in (b) to a plant to test for herbicidal activity; and
 - d) selecting a compound identified in (c) that has herbicidal activity.
- 2. The method according to claim 1, wherein said polypeptide comprises an amino acid sequence at least 95% identical to an amino acid sequence selected from the group consisting of the even numbered SEQ ID NOs:2-96.
- 3. The method according to claim 2, wherein said polypeptide comprises an amino acid sequence at least 99% identical to an amino acid sequence selected from the group consisting of the even numbered SEQ ID NOs:2-96.
- 4. The method according to claim 3, wherein said polypeptide comprises an amino acid sequence selected from the group consisting of the even numbered SEQ ID NOs:2-96.
 - 5. A method of identifying a herbicidal compound, comprising:
 - c) combining a polypeptide comprising an amino acid sequence at least 90% identical to an amino acid sequence selected from the group consisting of the even numbered SEQ ID NOs:2-96 with a compound to be tested for the ability to inhibit the activity of said polypeptide, under conditions conducive to inhibition;
 - d) selecting a compound identified in (a) that inhibits the activity of said polypeptide;
 - c) applying a compound selected in (b) to a plant to test for herbicidal activity; and
 - d) selecting a compound identified in (c) that has herbicidal activity.

6. The method according to claim 5, wherein said polypeptide comprises an amino acid sequence at least 95% identical to an amino acid sequence selected from the group consisting of the even numbered SEQ ID NOs:2-96.

- 7. The method according to claim 6, wherein said polypeptide comprises an amino acid sequence at least 99% identical to an amino acid sequence selected from the group consisting of the even numbered SEQ ID NOs:2-96.
- 8. The method according to claim 7, wherein said polypeptide comprises an amino acid sequence selected from the group consisting of the even numbered SEQ ID NOs:2-96.
 - 9. A method for killing or inhibiting the growth or viability of a plant, comprising applying to the plant a herbicidal compound identified according to the method of claim 1.
- 15 10. A method for killing or inhibiting the growth or viability of a plant, comprising applying to the plant a herbicidal compound identified according to the method of claim 5.

SEQUENCE LISTING

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Phe Val Ile Glu Arg Ile Asp Glu His Lys Gly Thr Tyr Ser Ile Ala 130 135 140

Pro Leu Leu Leu Ala Gly Leu Val Ser Ile Leu Tyr Trp Arg Phe Phe 145 150 155 160

Asp Asp Leu Arg Pro Tyr Ala Leu Val Gln Phe Val Pro Cys Ile Val 165 170 175

Ile Pro Leu Met Ala Ile Leu Leu Pro Pro Met Tyr Thr His Ser Thr 180 185 190

Tyr Trp Leu Trp Ala Ala Gly Phe Tyr Leu Leu Ala Lys Val Glu Glu 195 200 205

Ala Ala Asp Lys Pro Ile Tyr Ser Trp Thr His His Ile Ile Ser Gly
210 215 220

His Ser Leu Lys His Leu Cys Ala Ala Met Val Pro Val Phe Leu Thr 225 230 235 240

Leu Met Leu Ala Lys Arg Thr Val Gln Thr Glu Arg Ile Ser Leu Tyr 245 250 255

Lys Thr Trp Lys Lys Gly Ser Glu Glu Glu Arg Phe Glu His Ser Tyr 260 265 270

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gcc Ala	aag Lys	tat Tyr 35	gga Gly	ctg Leu	gga Gly	gct Ala	acc Thr 40	cgg Arg	aaa Lys	aaa Lys	cag Gln	ctc Leu 45	ttt Phe	cga Arg	gtc Val	144
tat Tyr	gcg Ala 50	tct Ser	gaa Glu	agt Ser	agt Ser	agt Ser 55	eja aaa	tct Ser	tca Ser	tct Ser	aat Asn 60	agc Ser	gat Asp	gga Gly	ggc Gly	192
ttt Phe 65	tcg Ser	tgg Trp	gtg Val	aga Arg	ttg Leu 70	gct Ala	cag Gln	tct Ser	att Ile	cgc Arg 75	ctt Leu	ggt Gly	gcc Ala	gag Glu	cgg Arg 80	240
att Ile	Gly 999	gag Glu	aag Lys	att Ile 85	gga Gly	gaa Glu	tct Ser	gtg Val	aag Lys 90	aca Thr	gaa Glu	att Ile	GJA aaa	ttt Phe 95	gac Asp	288
tcg Ser	gaa Glu	gaa Glu	gca Ala 100	agt Ser	glà aaa	aga Arg	gtg Val	aat Asn 105	Glu	tat Tyr	gtg Val	gct Ala	cga Arg 110	gtt Val	aag Lys	336
gat Asp	agt Ser	gtg Val 115	cac His	aag Lys	ggc Gly	cat His	cac His 120	gag Glu	ctg Leu	act Thr	cgc Arg	ttt Phe 125	Lys	aat Asn	gag Glu	384
aca Thr	gtg Val 130	cct Pro	tcg Ser	ttt Phe	att Ile	gat Asp 135	tgg Trp	aac Asn	aag Lys	tgg Trp	gag Glu 140	His	tgg Trp	aag Lys	gac	432
atc Ile 145	Arg	aat Asn	tgg Trp	gac Asp	ggt Gly 150	aaa Lys	cga Arg	gtt Val	gct Ala	gcc Ala 155	ttg Leu	tto Phe	ata Ile	tat Tyr	gct Ala 160	480
ttt Phe	gcg Ala	ctg Leu	tta Leu	ctt Leu 165	Ser	tgt Cys	caa Gln	aga Arg	gtt Val 170	Tyr	gtt Val	gcc Ala	ato Ile	caa Glr 175	gct Ala	528
cct	cgg Arg	gta Val	gaa Glu 180	Arg	gag Glu	aga Arg	aga Arg	gag Glu 185	ı Lev	aca Thr	gag Glu	tct Ser	ttt Phe 190	Met	g gag : Glu	576
gct	ttg Leu	ato Ile 195	Pro	gag Glu	cca Pro	tct Ser	Pro 200	Ġl3	a aat 7 Asr	ata lle	gaa Glu	a aag 1 Lys 205	s Phe	aag Lys	aga Arg	624
aat Asr	ato Met 210	Trp	agg Arg	aaa Lys	gca Ala	aca Thr 215	Pro	aaa Ly:	a ggo s Gly	ttg / Lev	g aaa Lys 220	s Let	a aaa u Lys	a agg	g ttc g Phe	672
att Ile 225	e Glu	gco Ala	ect Pro	gat Asp	gga Gly 230	Thr	ctt Lev	gto 1 Va	c cad l His	gat S Asp 235	Se	t tc r Se:	t tai	t gt r Val	t gga l Gly 240	720
gaa	a aat	gcg	g tgg	gat	gac	gat	cta	a ga	g acc	e aca	a ga	g gg:	a tc	t ct	c aag	768

Glu	Asn	Ala	Trp	Asp 245	Asp	Asp	Leu	Glu	Thr 250	Thr	Glu	Gly	Ser	Leu 255	Lys	
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aga Arg 385	Leu	tat Tyr	gtg Val	acc	atg Met	Lys	gaa Glu	ggt Gly	ttc Phe	cct Pro	Lev	ı gaa ı Glu	tat Tyr	att Tle	gtt Val 400	1200
gac Asp	att Ile	ccc Pro	tta Leu	gat Asp 405	Pro	tac Tyr	tto Lev	ttt Phe	gag Glu	ı Thr	att Ile	tgo Cys	aac Ası	gce n Ala 41	gga Gly	1248
gtt Val	gag Glu	gto Val	g gat L Asp 420	Lev	ctt Leu	cag ıGlr	g aag Lys	g agg s Arg 429	g Glr	g ato n Ile	c cad	tac Tyn	Pho 430	e Me	g aaa t Lys	1296
gtt Va]	tto Phe	att 110 43!	a Ala	ctt Lei	cto Lei	g ccg	999 Gly	y Ile	a cta e Lei	a att ı Ile	tta E Le	a tgg u Trj 44!	p Ph	t at e Il	a aga e Arg	1344
gaa Glu	1 tct 1 Se1 450	Ala	c atg a Met	g ctt Lei	cto Le	c ctt ı Lei 45!	ı Il	c ace	a tco r Se:	c aag r Lyg	g cg s Ar 46	g Ph	t ct e Le	c ta u Ty	c aag r Lys	1392
aag Ly: 46!	з Ту	aat Asi	t caq n Gli	g cto n Lei	g tt: 1 Pho 47	e Asj	t at	g gc t Al	t ta a Ty	t gc r Al 47	a Gl	a aa u As	t tt n Ph	t at e Il	a ttg e Leu 480	1440
cc	g gt:	t gg	a gat	t gt	c ag	t ga	g ac	a aa	a tc	a at	g ta	t aa	g ga	a gt	g gta	1488

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	ata Ile	gac Asp 690	Phe	: Gly	aag Lys	g ctt Leu	gtt Val 695	Phe	cga Arg	a acg g Thi	g gti r Va:	t gg 1 Gl ₃ 700	y Pho	t tco e Sei	c ggg	g gca y Ala	2112
	gat Asp 705	ıle	cgg Arg	aat Asn	ctt Lev	gtt Va] 710	Ası	gaa Glu	a gcg ı Ala	g get a Ala	t ata a Ilo 71	e Me	g to t Se	g gta	a agg	g aag g Lys 720	2160
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980

985

990

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Tyr Ala Ser Glu Ser Ser Ser Gly Ser Ser Ser Asn Ser Asp Gly Gly 50 55 60

Phe Ser Trp Val Arg Leu Ala Gln Ser Ile Arg Leu Gly Ala Glu Arg 65 70 75 80

Ile Gly Glu Lys Ile Gly Glu Ser Val Lys Thr Glu Ile Gly Phe Asp 85 90 95

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Asp Ser Val His Lys Gly His His Glu Leu Thr Arg Phe Lys Asn Glu 115 120 125

Thr Val Pro Ser Phe Ile Asp Trp Asn Lys Trp Glu His Trp Lys Asp 130 135 140

Ile Arg Asn Trp Asp Gly Lys Arg Val Ala Ala Leu Phe Ile Tyr Ala 145 150 155 160

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- Lys Ile Ile Gly Arg Asn Ala Arg Ile Gln Thr Glu Ala Lys Lys Lys 260 265 270
- Leu Ser Gln Asp Leu Gly Val Ser Gly Glu Ile Gly Asp Ser Val Gly 275 280 285
- Asn Trp Arg Glu Arg Leu Ala Thr Trp Lys Glu Met Leu Glu Arg Glu 290 295 300
- Lys Leu Ser Glu Gln Leu Asn Ser Ser Ala Ala Lys Tyr Val Val Glu 305 310 315 320
- Phe Asp Met Lys Glu Val Glu Lys Ser Leu Arg Glu Asp Val Ile Gly 325 330 335
- Arg Thr Ser Glu Thr Glu Gly Thr Arg Ala Leu Trp Ile Ser Lys Arg 340 345 350
- Trp Trp Arg Tyr Arg Pro Lys Leu Pro Tyr Thr Tyr Phe Leu Gln Lys 355 360 365
- Leu Asp Ser Ser Glu Val Ala Ala Val Val Phe Thr Glu Asp Leu Lys 370 375 380

Arg Leu Tyr Val Thr Met Lys Glu Gly Phe Pro Leu Glu Tyr Ile Val 385 390 395 400

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Val Glu Val Asp Leu Gln Lys Arg Gln Ile His Tyr Phe Met Lys 420 425 430

Val Phe Ile Ala Leu Leu Pro Gly Ile Leu Ile Leu Trp Phe Ile Arg 435 440 445

Glu Ser Ala Met Leu Leu Leu Ile Thr Ser Lys Arg Phe Leu Tyr Lys 450 455 460

Lys Tyr Asn Gln Leu Phe Asp Met Ala Tyr Ala Glu Asn Phe Ile Leu 465 470 475 480

Pro Val Gly Asp Val Ser Glu Thr Lys Ser Met Tyr Lys Glu Val Val 485 490 495

Leu Gly Gly Asp Val Trp Asp Leu Leu Asp Glu Leu Met Ile Tyr Met 500 505 510

Gly Asn Pro Met Gln Tyr Tyr Glu Lys Asp Val Ala Phe Val Arg Gly 515 520 525

Val Leu Leu Ser Gly Pro Pro Gly Thr Gly Lys Thr Leu Phe Ala Arg 530 535 540

Thr Leu Ala Lys Glu Ser Gly Leu Pro Phe Val Phe Ala Ser Gly Ala 545 550 555 560

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Phe Ser Ile Ala Arg Arg Asn Ala Pro Ala Phe Val Phe Val Asp Glu 580 585 590

Ile Asp Ala Ile Ala Gly Arg His Ala Arg Lys Asp Pro Arg Arg Arg 595 600 605

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- Arg Ile Asp Arg Arg Leu Tyr Ile Gly Leu Pro Asp Ala Lys Gln Arg 660 665 670
- Val Gln Ile Phe Gly Val His Ser Ala Gly Lys Asn Leu Ala Glu Asp 675 680 685
- Ile Asp Phe Gly Lys Leu Val Phe Arg Thr Val Gly Phe Ser Gly Ala 690 695 700
- Asp Ile Arg Asn Leu Val Asn Glu Ala Ala Ile Met Ser Val Arg Lys 705 710 715 720
- Gly Arg Ser Tyr Ile Tyr Gln Gln Asp Ile Val Asp Val Leu Asp Lys 725 730 735
- Gln Leu Leu Glu Gly Met Gly Val Leu Leu Thr Glu Glu Glu Gln Gln 740 745 750
- Lys Cys Glu Gln Ser Val Ser Tyr Glu Lys Lys Arg Leu Leu Ala Val 755 760 765
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- Trp His Ala Phe Ser Gln Leu Leu Pro Gly Gly Lys Glu Thr Ala Val 785 790 795 800
- Ser Val Phe Tyr Pro Arg Glu Asp Met Val Asp Gln Gly Tyr Thr Thr 805 810 815
- Phe Gly Tyr Met Lys Met Gln Met Val Val Ala His Gly Gly Arg Cys 820 825 830
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Gln Ser Ala Arg Leu Gly Leu Thr Gln Leu Val Lys Lys Ile Gly Met 865 870 875 880

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Asp His Pro His Val Met Pro Ala Glu Met Ser Val Glu Val Ser Glu 900 905 910

Leu Phe Thr Arg Glu Leu Thr Arg Tyr Ile Glu Glu Thr Glu Glu Leu 915 920 925

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					ctt Leu												336
					cac His												384
					ggt Gly												432
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					cct Pro										tgg Trp		528
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								Arg					Thr		atc Ile		624
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							ttg Leu 360								gat Asp	. 1	L104
							aac Asn									j	1152 [.]
							gaa Glu									:	1200
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	Lys				_		_		_		Glr		_		yal Val 480		1440
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aga Arg	atg Met	aag Lys 595	Lys	tac Tyr	gaa Glu	atc Ile	gaa Glu 600	Pro	ccg Pro	ctt Leu	atg Met	gaa Glu 605	aag Lys	ctt Leu	gat Asp	1824
tac Tyr	atc Ile 610	ctg Leu	agc Ser	ttg Leu	aag Lys	aaa Lys 615	aaa Lys	gag Glu	gtg Val	aag Lys	aag Lys 620	Arg	ccg Pro	ttt Phe	agc Ser	1872
atg Met 625	Lys	cta Leu	agc Ser	aaa Lys	gac Asp 630	Gln	cgt Arg	gag Glu	gta Val	ttg Leu 635	Val	ggt Gly	ttg Leu	ttg Leu	tta Leu 640	1920
ggt Gly	ggc	ttg Leu	caa Gln	atc Ile 645	Glu	tca Ser	gac Asp	aaa Lys	gag Glu 650	. Lys	aag Lys	g ago s Ser	cac His	ato Met 655	atc : Ile	1968
aaa Lys	ttt Phe	gaa Glu	ttt Phe 660	Arg	gaa Glu	aat Asn	tct Ser	caa Glr 669	ı Ala	cat His	ctg Lei	g gtt 1 Val	ctt L Lev 670	і Гуз	a caa s Gln	2016
aac Asr	ata Ile	cat His	Asp	cac Glr	tto Phe	cgt Arc	gag Gli 680	ı Try	g ttg p Lei	g cat 1 His	cci Pro	t ttg b Lei 68!	ı Sei	c aat	ttt n Phe	2064
caç Glr	gag Glu 690	Asp	atto Ile	ata E Ile	e Pro	tto Phe 695	e Glu	a tto ı Pho	e tac	c tco c Sei	gt Va 70	l Pro	c cat o His	t tca s Se:	a tac r Tyr	2112
tto Phe 705	Gly	ttt Phe	tac Tyr	gct Ala	gaa Glu 710	ı His	tac Ty	c tgg r Trj	g cca p Pro	a aaq 5 Ly: 71!	s Gl	t cag	g cca n Pro	a ga	g att u Ile 720	2160
cca	a aaa	ctg	g att	cat	cgg	tgg	g cta	a tc	g cc	a ca	c tc	a ct	c gc	g ta	t tgg	2208

Pro Lys	Leu I	le His 725	Arg '	Trp	Leu		Pro 730	His	Ser	Leu	Ala	Tyr 735	Trp	
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ttg aag Leu Lys	gga a Gly S 755	gt ctc er Leu	gaa Glu	ggt Gly	gtt Val 760	gag Glu	aaa Lys	gta Val	gta Val	aag Lys 765	gct Ala	ctt Leu	caa Gln	2304
gcc aaa Ala Lys 770	Ser M	tg gaa et Glu	Cys	cga Arg 775	gtt Val	aag Lys	aag Lys	aaa Lys	gga Gly 780	aaa Lys	gtc Val	ttc Phe	tgg Trp	2352
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cct cat Pro His	gtg t Val L	ta gag eu Glu 805	aac Asn	ttg Leu	aaa Lys	gag Glu	cat His 810	ttg Leu	aaa Lys	cct Pro	gct Ala	tct Ser 815	gaa Glu	2448
tca ctg Ser Leu	Asp A	at gtt Asn Val 320	aag Lys	gaa Glu	gca Ala	gaa Glu 825	gaa Glu	caa Gln	agc Ser	atc Ile	aac Asn 830	ttc Phe	aaa Lys	2496
tca aac Ser Asr	tct g Ser A 835	at cac Asp His	agt Ser	gac Asp	gat Asp 840	tgt Cys	gtc Val	aat Asn	tca Ser	gaa Glu 845	gca Ala	cat His	ttt Phe	2544
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Ile Ile Asn Ser Ser Ser Thr Leu Phe Arg Ser Leu Ser Phe Ser Leu 50 55 60

- Ile Arg His Arg Ser Ser Tyr Ser Arg Arg Ser Leu Arg Arg Leu Ser 65 70 75 80
- Ile His Thr Val His Gly Asn Lys Thr Gln Phe Phe Ser His Ser Ser 85 90 95
- Thr Arg Thr Pro Pro Leu Phe Thr Ala Asn Ser Thr Ala Gln Arg Ser 100 105 110
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 115 120 125
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- Ile Arg Asn Val Ala Thr Arg Arg Ile Glu Thr Glu Phe Glu Val Arg 145 150 155 160
- Glu Leu Glu Glu Leu Pro Glu Glu Trp Arg Arg Ser Lys Leu Ala Trp 165 170 175
- Leu Cys Lys Glu Val Pro Thr His Lys Ala Val Thr Leu Val Arg Leu 180 185 190
- Leu Asn Ala Gln Lys Lys Trp Val Arg Gln Glu Asp Ala Thr Tyr Ile 195 200 205
- Ser Val His Cys Met Arg Ile Arg Glu Asn Glu Thr Gly Phe Arg Val 210 215 220
- Tyr Arg Trp Met Thr Gln Gln Asn Trp Tyr Arg Phe Asp Phe Gly Leu 225 230 235 240
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- Cys Arg Glu Val Phe Asp Asp Val Leu Asn Gln Gly Arg Val Pro Ser 260 265 270
- Glu Ser Thr Phe His Ile Leu Val Val Ala Tyr Leu Ser Ser Leu Ser 275 280 285

Val Glu Gly Cys Leu Glu Glu Ala Cys Ser Val Tyr Asn Arg Met Ile 290 295 300

Gln Leu Gly Gly Tyr Lys Pro Arg Leu Ser Leu His Asn Ser Leu Phe 305 310 315 320

Arg Ala Leu Val Ser Lys Gln Gly Gly Ile Leu Asn Asp Gln Leu Lys 325 330 335

Gln Ala Glu Phe Ile Phe His Asn Val Val Thr Thr Gly Leu Glu Val 340 345 350

Gln Lys Asp Ile Tyr Ser Gly Leu Ile Trp Leu His Ser Cys Gln Asp 355 360 365

Glu Val Asp Ile Gly Arg Ile Asn Ser Leu Arg Glu Glu Met Lys Lys 370 375 380

Ala Gly Phe Gln Glu Ser Lys Glu Val Val Val Ser Leu Leu Arg Ala 385 390 395 400

Tyr Ala Lys Glu Gly Gly Val Glu Glu Val Glu Arg Thr Trp Leu Glu
405 410 415

Leu Leu Asp Leu Asp Cys Gly Ile Pro Ser Gln Ala Phe Val Tyr Lys
420 425 430

Ile Glu Ala Tyr Ser Lys Val Gly Asp Phe Ala Lys Ala Met Glu Ile 435 440 445

Phe Arg Glu Met Glu Lys His Ile Gly Gly Ala Thr Met Ser Gly Tyr 450 460

His Lys Ile Ile Glu Val Leu Cys Lys Val Gln Gln Val Glu Leu Val 465 470 475 480

Glu Thr Leu Met Lys Glu Phe Glu Glu Ser Gly Lys Lys Pro Leu Leu 485 490 495

Pro Ser Phe Ile Glu Ile Ala Lys Met Tyr Phe Asp Leu Gly Leu His 500 505 510

Glu Lys Leu Glu Met Ala Phe Val Gln Cys Leu Glu Lys Cys Gln Pro 515 520 525 WO 03/008440 PCT/EP02/07929 ·

Ser Gln Pro Ile Tyr Asn Ile Tyr Leu Asp Ser Leu Thr Lys Ile Gly 530 535 540

Asn Leu Glu Lys Ala Gly Asp Val Phe Asn Glu Met Lys Asn Asn Gly 545 550 555 560

Thr Ile Asn Val Ser Ala Arg Ser Cys Asn Ser Leu Leu Lys Gly Tyr 565 570 575

Leu Asp Cys Gly Lys Gln Val Gln Ala Glu Arg Ile Tyr Asp Leu Met 580 585 590

Arg Met Lys Lys Tyr Glu Ile Glu Pro Pro Leu Met Glu Lys Leu Asp 595 600 605

Tyr Ile Leu Ser Leu Lys Lys Glu Val Lys Lys Arg Pro Phe Ser 610 620

Met Lys Leu Ser Lys Asp Gln Arg Glu Val Leu Val Gly Leu Leu 625 630 635 640

Gly Gly Leu Gln Ile Glu Ser Asp Lys Glu Lys Lys Ser His Met Ile 645 650 655

Lys Phe Glu Phe Arg Glu Asn Ser Gln Ala His Leu Val Leu Lys Gln 660 665 670

Asn Ile His Asp Gln Phe Arg Glu Trp Leu His Pro Leu Ser Asn Phe 675 680 685

Gln Glu Asp Ile Ile Pro Phe Glu Phe Tyr Ser Val Pro His Ser Tyr 690 695 700

Phe Gly Phe Tyr Ala Glu His Tyr Trp Pro Lys Gly Gln Pro Glu Ile 705 710 715 720

Pro Lys Leu Ile His Arg Trp Leu Ser Pro His Ser Leu Ala Tyr Trp
725 730 735

Tyr Met Tyr Ser Gly Val Lys Thr Ser Ser Gly Asp Ile Ile Leu Arg 740 745 750

Leu Lys Gly Ser Leu Glu Gly Val Glu Lys Val Val Lys Ala Leu Gln 755 760 765

Ala Lys Ser Met Glu Cys Arg Val Lys Lys Lys Gly Lys Val Phe Trp 770 Ile Gly Leu Gln Gly Thr Asn Ser Ala Leu Phe Trp Lys Leu Ile Glu 790 Pro His Val Leu Glu Asn Leu Lys Glu His Leu Lys Pro Ala Ser Glu 810 Ser Leu Asp Asn Val Lys Glu Ala Glu Glu Gln Ser Ile Asn Phe Lys Ser Asn Ser Asp His Ser Asp Asp Cys Val Asn Ser Glu Ala His Phe 840 Tyr <210> 9 <211> 1449 <212> DNA <213> Arabidopsis thaliana <220> <221> CDS <222> (1)..(1449) <223> 8794 <400> 9 atg gtt gga tct ttg gaa tct gat caa act ctt tca atg gcc acc tta 48 Met Val Gly Ser Leu Glu Ser Asp Gln Thr Leu Ser Met Ala Thr Leu 96 ate gaa aaa ete gae ate tta tet gae gae tte gat eea ace gee gta Ile Glu Lys Leu Asp Ile Leu Ser Asp Asp Phe Asp Pro Thr Ala Val 20 25 144 gtc acc gaa ccg tta cct cct ccg gta act aat gga atc gga gct gat Val Thr Glu Pro Leu Pro Pro Pro Val Thr Asn Gly Ile Gly Ala Asp 35 aaa gga gga gga gga gaa aga gag atg gtt ctc ggt agg aat ata . 192 Lys Gly Gly Gly Gly Glu Arg Glu Met Val Leu Gly Arg Asn Ile

50

	•															
cac His 65	aca Thr	acg Thr	tca Ser	ctc Leu	gct Ala 70	gta Val	acg Thr	gaa Glu	ccg Pro	gag Glu 75	gtt Val	aac Asn	gat Asp	gaa Glu	ttc Phe 80	240
acc Thr	gga Gly	gat Asp	aaa Lys	gaa Glu 85	gct Ala	tat Tyr	atg Met	gct Ala	agt Ser 90	gtt Val	ctt Leu	gct Ala	cgt Arg	tac Tyr 95	cgg Arg	288
aaa Lys	act Thr	ttg Leu	gtt Val 100	gaa Glu	cga Arg	acc Thr	aaa Lys	aac Asn 105	cat His	tta Leu	ggt Gly	tat Tyr	cct Pro 110	tat Tyr	aac Asn	336
ttg Leu	gat Asp	ttc Phe 115	gac Asp	tat Tyr	ggt Gly	gcg Ala	ctt Leu 120	ggt Gly	cag Gln	tta Leu	caa Gln	cat His 125	ttt Phe	tcg Ser	att Ile	384
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aga Arg 145	cct Pro	ttt Phe	gaa Glu	gtt Val	ggt Gly 150	gtg Val	ttg Leu	gat Asp	tgg Trp	ttt Phe 155	Ala	cgt Arg	ctt Leu	tgg Trp	gag Glu 160	480
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ggc Gly	aac Asn	ctt Leu	cat His 180	ggc	att Ile	tta Leu	gtc Val	999 Gly 185	Arg	gag Glu	atg Met	ttt: Phe	ccc Pro	As _I	gly ggg	576
ata Ile	ttg Leu	tat Tyr 195	Ala	tcg Ser	cgt Arg	gaa Glu	tcc Ser 200	His	tac Tyr	tcg Ser	gtg Val	ttt L Phe 205	E Lys	a gct s Ala	gct a Ala	624
cga Arg	atg Met 210	Тут	cga Arg	atg Met	gag Glu	tgt Cys 215	Glı	g aag 1 Lys	gtt Val	gat L Asp	220	r Lei	ato 1 Mei	g tc: t Se:	a ggg r Gly	672
gag Glu 225	ı Ile	gat Asp	tgt Cys	gat Asp	gat Asp 230	Leu	agg Arg	g aag g Lys	g aag s Lys	g ttg s Lem 23!	a Le	g gct u Ala	t aa a As:	t aa n Ly	a gat s Asp 240	720
aaa Lys	a ccg	gcg Ala	g att a Ile	ctt Lev 245	ı Asr	gtt Val	aa Asi	c ata n Ile	a gga e Gl; 25	y Th	g ac r Th	g gt r Va	t aa l Ly	a gg s Gl 25	a gct y Ala 5	768
gti Va	gat L Asp	gai Asj	ctt Lei 260	ı Asp	c ctt p Lei	gtt 1 Val	ate III	c aaa e Lya 26	s Th	t ct r Le	t ga u Gl	a ga u Gl	g tg u Cy 27	s G1	t ttc y Phe	816
tc: Se:	a cat r His	ga: S As; 27:	p Ar	g tto	c tat	t att	c ca Hi 28	в Су	t ga s As	t gg p Gl	a go y Al	t tt a Le 28	u Ph	t gg le G]	ya ctt y Leu	864
at Me	g ato t Med 290	t Pr	t tti	t gte e Vai	c aaa l Lys	a cgi s Arg 29	g Al	a cc a Pr	g aa o Ly	a gt s Va	g ac 1 Th 30	ir Ph	t aa 1e As	it aa sn Ly	a ccg /s Pro	912

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cca Pro	tgt Cys	ggt Gly	gtt Val	cag Gln 325	ata Ile	aca Thr	aga Arg	atg Met	gaa Glu 330	cat His	atc Ile	aaa Lys	gtc Val	ctc Leu 335	tcc Ser	1008
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					cag Gln											1152
					cga Arg 390											1200
					act Thr											1248
					cag Gln											1296
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Lys Gly Gly Gly Gly Glu Arg Glu Met Val Leu Gly Arg Asn Ile 50 55 60

His Thr Thr Ser Leu Ala Val Thr Glu Pro Glu Val Asn Asp Glu Phe 65 70 75 80

Thr Gly Asp Lys Glu Ala Tyr Met Ala Ser Val Leu Ala Arg Tyr Arg 85 90 95

Lys Thr Leu Val Glu Arg Thr Lys Asn His Leu Gly Tyr Pro Tyr Asn 100 105 110

Leu Asp Phe Asp Tyr Gly Ala Leu Gly Gln Leu Gln His Phe Ser Ile 115 120 125

Asn Asn Leu Gly Asp Pro Phe Ile Glu Ser Asn Tyr Gly Val His Ser

Arg Pro Phe Glu Val Gly Val Leu Asp Trp Phe Ala Arg Leu Trp Glu 145 150 155 160

Ile Glu Arg Asp Asp Tyr Trp Gly Tyr Ile Thr Asn Cys Gly Thr Glu 165 170 175

Gly Asn Leu His Gly Ile Leu Val Gly Arg Glu Met Phe Pro Asp Gly 180 185 190

Ile Leu Tyr Ala Ser Arg Glu Ser His Tyr Ser Val Phe Lys Ala Ala 195 200 205

Arg Met Tyr Arg Met Glu Cys Glu Lys Val Asp Thr Leu Met Ser Gly 210 215 220

Glu Ile Asp Cys Asp Asp Leu Arg Lys Lys Leu Leu Ala Asn Lys Asp 225 230 235 240

Lys Pro Ala Ile Leu Asn Val Asn Ile Gly Thr Thr Val Lys Gly Ala 245 250 255

Val Asp Asp Leu Asp Leu Val Ile Lys Thr Leu Glu Glu Cys Gly Phe 260 265 270

Ser His Asp Arg Phe Tyr Ile His Cys Asp Gly Ala Leu Phe Gly Leu 275 280 285

Met Met Pro Phe Val Lys Arg Ala Pro Lys Val Thr Phe Asn Lys Pro 290 295 300

Ile Gly Ser Val Ser Val Ser Gly His Lys Phe Val Gly Cys Pro Met 305 310 315 320

Pro Cys Gly Val Gln Ile Thr Arg Met Glu His Ile Lys Val Leu Ser 325 330 335

Ser Asn Val Glu Tyr Leu Ala Ser Arg Asp Ala Thr Ile Met Gly Ser 340 345 350

Arg Asn Gly His Ala Pro Leu Phe Leu Trp Tyr Thr Leu Asn Arg Lys 355 360 365

Gly Tyr Lys Gly Phe Gln Lys Glu Val Gln Lys Cys Leu Arg Asn Ala 370 375 380

His Tyr Leu Lys Asp Arg Leu Arg Glu Ala Gly Ile Ser Ala Met Leu 385 390 395 400

Asn Glu Leu Ser Ser Thr Val Val Phe Glu Arg Pro Lys Asp Glu Glu 405 410 415

Phe Val Arg Arg Trp Gln Leu Ala Cys Gln Gly Asp Ile Ala His Val 420 425 430

Val Val Met Pro Ser Val Thr Ile Glu Lys Leu Asp Asn Phe Leu Lys 435 440 445

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Pro Cys Leu Ala Ser Glu Val Gly Thr Asn Asn Cys Ile Cys Pro Ala 465 470 475 480

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Cys Arg Pro Leu Ser Lys Thr Val Arg Phe Asn Val Leu Lys Val Ile 130 135 140

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Asn Arg Phe Trp Lys Asn Ile Gly Leu Gly Phe Lys Thr Pro Arg Glu 35 40 45

Ala Ile Asp Gly Ala Tyr Val Asp Lys Lys Cys Pro Phe Thr Gly Thr 50 55 60

Val Ser Ile Arg Gly Arg Ile Leu Ala Gly Thr Cys. His Ser Ala Lys 65 70 75 80

Met Gln Arg Thr Ile Ile Val Arg Arg Asp Tyr Leu His Phe Val Lys 85 90 95

Lys Tyr Gln Arg Tyr Glu Lys Arg His Ser Asn Ile Pro Ala His Val 100 105 110

Ser Pro Cys Phe Arg Val Lys Glu Gly Asp His Ile Ile Gly Gln 115 120 125

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Pro Ala Gly Ser Ser Ser Phe Gly Lys Lys Ala Phe Thr Gly Met 145 150 155 160

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	ca :	aaa	220	202	act :	aac	cqt	cac	aga	gga	aag	gtg	aag	gcg	ttc	96
Leu P	ro	Arg	Lys 20	Arg	Ala i	Asn .	Arg	His 25	Arg	Gly	Lys	Val	Lys 30	Ala	Phe	
cct a	aa ·	qat	~~~	caa	acc	aag	cct	tgc	aag	ttc	aca	gct	ttc	atg	ggt	144
Pro L	ys .	Asp 35	Asp	Gln	Thr	Lys	Pro 40	Cys	Lys	Phe	Thr	A1a 45	Pne	мес	GIA	
tac a	aaa	gct	ggt	atg	act	cac	att	gtc	aga	gaa	gtg	gag	aaa	cct	gga	192
Tyr I	Lys 50	Ala	Gly	Met	Thr	His 55	Ile	Val	Arg	GIu	60	GIU	пув	PIO	Сту	
tec a	aag	ctt	cac	aag	aag	gag	aca	tgt	gag	gct	gtt	acc	atc	att	gag	240
Ser I	ГÀЗ	Leu	His	Lys	Lys 70	Glu	Thr	Cys	GIU	75	val	7111	110	110	80	
aca (cct	gct	atg	gtg	gtt	gtt	gga	gtt	gtt	gcc	tat	gtg Val	aag Lvs	act	cct	288
Thr	Pro	Ala	Met	Val 85	Val	vaı	GIY	vai	90	AIG	. Iyi	vas		95		
aga (ggt	ttg	agg	tct	ttg	aac	act	gtc	tgg	gca Nala	cag	cat	ttg Lev	g agt L Ser	gag Glu	336
Arg	Gly	Leu	100	ser	ьeu	ASII	1111	105	*-1	, mi	. 0		110)		
gag	gtc	agg	aga	agg	ttc	tac	aag	aac Asn	tgg	g gct	aag Lvs	tct Se:	aag Lys	g aag s Lys	aag Lys	384
GIU	vaı	115		Arg	FIIC	TYT	120)			•	12	5	_		
gct	ttc	act	. ggg	tac	gct	aag	cag	tat	gad Asi	c agt	gaç r Glı	g gai	t ggd p Gl	c aaq y Ly:	g aag s Lys	432
ALA	130		. вту	TYL	ATO	135	,	<i>1</i> -			140	o '				
ggt	att	caç	ggct	cag	ctt	gag	aag	g ato	g aa	g aa	g tad	gc gc	t ac	t gt	c atc	480

Gly 145	Ile	Gln	Ala	Gln	Leu 150	Glu	Lys	Met	Lys	Lys 155	Tyr	Ala	Thr	Val	Ile 160	
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			gac Asp													624
gaa Glu	gct Ala 210	gtc Val	ttc Phe	cag Gln	aag Lys	gat Asp 215	gaa Glu	atg Met	att Ile	gat Asp	atc Ile 220	att Ile	ggt Gly	gtg Val	acc Thr	672
aag Lys 225	ggt Gly	aag Lys	ggt Gly	tat Tyr	gaa Glu 230	ggt Gly	gtt Val	gtt Val	act Thr	cgt Arg 235	tgg Trp	ggt Gly	gtt Val	acc Thr	cgt Arg 240	720
			aag Lys													768
gcg Ala	tgg Trp	cat His	cct Pro 260	gct Ala	aga Arg	gtg Val	tcc Ser	tac Tyr 265	act Thr	gtt Val	gct Ala	agg Arg	gct Ala 270	ggt	cag Gln	816
aac Asn	ggt Gly	tac Tyr 275	cat His	cac His	cgt Arg	act Thr	gag Glu 280	Leu	aac Asn	aag Lys	aag Lys	att Ile 285	tac Tyr	agg Arg	ttg Leu	864
ggt Gly	aag Lys 290	gtt Val	ggt Gly	act Thr	gag Glu	gca Ala 295	cac His	aca Thr	gcc	atg Met	act Thr 300	Glu	tat Tyr	gac Asp	agg Arg	912
	Glu										Pro				att Ile 320	960
gtg Val	aag Lys	gat Asp	gac Asp	tac Tyr 325	Leu	atg Met	att Ile	aag Lys	Gly	Cys	tgt Cys	gtt Val	ggt Gly	Pro 335	aag Lys	1008
				Thr					Leu					Ser	Arg	1056
ctt Lev	gcc Ala	ttg Leu 355	Glu	gag Glu	atc Ile	aaa Lys	Leu 360	. Lys	ttt Phe	att Ile	gac Asp	acc Thr 365	Ala	tco a Ser	att Ile	1104
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Tyr Lys Ala Gly Met Thr His Ile Val Arg Glu Val Glu Lys Pro Gly
50 55 60

Ser Lys Leu His Lys Lys Glu Thr Cys Glu Ala Val Thr Ile Ile Glu 65 70 75 80

Thr Pro Ala Met Val Val Val Gly Val Val Ala Tyr Val Lys Thr Pro 85 90 95

Arg Gly Leu Arg Ser Leu Asn Thr Val Trp Ala Gln His Leu Ser Glu 100 105 110

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Ala Phe Thr Gly Tyr Ala Lys Gln Tyr Asp Ser Glu Asp Gly Lys Lys 130 135 140

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Arg Val Leu Ala His Thr Gln Ile Arg Lys Met Lys Gly Leu Lys Gln 165 170 175

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Glu Ala Val Phe Gln Lys Asp Glu Met Ile Asp Ile Ile Gly Val Thr 210 215 220

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Ala Trp His Pro Ala Arg Val Ser Tyr Thr Val Ala Arg Ala Gly Gln 260 265 270

Asn Gly Tyr His His Arg Thr Glu Leu Asn Lys Lys Ile Tyr Arg Leu 275 280 285

Gly Lys Val Gly Thr Glu Ala His Thr Ala Met Thr Glu Tyr Asp Arg 290 295 300

Thr Glu Lys Asp Val Thr Pro Met Gly Gly Phe Pro His Tyr Gly Ile 305 310 315 320

Val Lys Asp Asp Tyr Leu Met Ile Lys Gly Cys Cys Val Gly Pro Lys 325 330 335

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Cys Asn Ile Gly Asp Arg Val Lys Leu Asp Pro Ser Arg Pro Leu Ser 50 55 60

Lys Asn Lys His Trp Ile Val Ala Glu Ile Ile Lys Lys Ala Arg Ile 65 70 75 80

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96

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gct Ala	gc a Al 21	a Le	c gc u Al	t ga a As	t aca p Th	a gt r Va 21	IAI	t a <u>c</u> .a Ar	ga ta ng Ty	ac c /r P	IO (tc g al 2 220	gat Asp	att Ile	c ca e Gl	ag ln	cca Pro	672
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Ala Ala Leu Val Asn Lys Gln Leu Arg Ser Ser Ser Tyr Asp Leu Asp 100 105 110

Val Lys Lys Pro Gln Asp Val Val Leu Pro Gly Ser Leu Ser Leu Leu 115 120 125

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Gly Pro Asn Ala Ser His Ile Thr Pro Met Ala Leu Asp Arg Trp Glu 180 185 190

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Ala Ala Leu Ala Asp Thr Val Ala Arg Tyr Pro Val Asp Ile Gln Pro 210 215 220

Phe Arg Asp Met Ile Glu Gly Met Arg Met Asp Leu Lys Lys Ser Arg 225 230 . 235 240

Tyr Gln Asn Phe Asp Asp Leu Tyr Leu Tyr Cys Tyr Tyr Val Ala Gly 245 250 255

Thr Val Gly Leu Met Ser Val Pro Val Met Gly Ile Asp Pro Lys Ser

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Ala Asn Gln Leu Thr Asn Ile Leu Arg Asp Val Gly Glu Asp Ala Arg 290 295 300

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cto Lev	cac His	Lys	ı gaa s Glı	att ı Ile	att Ile	gaç Glu 219	ı Le	a agg	g ga	a tto u Pho	c ac e Th 22	r Gl	c tta y Le	a ct u Le	t aac u Asn	672

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						ttt Phe										816
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Lys Glu Asp Thr Asn Lys Glu Val Ser Val Thr Val Arg Leu Tyr Gly 85 90 95

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ga As	t gg p Gl	t gt y Va	t aa l As	t at n Il 24	e Va	t ga l Gl	a ag u Ar	a ga g Gl	a gg u Gl 25	у І.	c ag Le S	gc t er P	tt a he <i>P</i>	ra Jag	ca Hi 25	S PI	g 768 o
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- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments
- (88) Date of publication of the international search report: 1 April 2004

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: NUCLEIC ACID MOLECULES ENCODING PROTEINS ESSENTIAL FOR PLANT GROWTH

(57) Abstract: Nucleotide sequences are isolated from Arabidopsis thaliana that code for proteins essential for plant growth and developement. The essentially of the proteins may be exploited by recombinantly expressing the proteins and using them in screening assays to identify compounds that interact with or inhibit the proteins and are therefore potential herbicides.

A. CLASSIFICATION OF SUBJECT MATTER IPC 7 G01N33/68 C12Q1/68

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols) I PC 7 C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, EMBASE, WPI Data, PAJ, Sequence Search, CHEM ABS Data

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE EMBL [Online] 1 March 2001 (2001-03-01), XP002253634 accession no. EBI Database accession no. Q9FKB8 abstract & KOTANI, H. ET AL: "Structural analysis of Arabidopsis thaliana chromosome 5. VI. Sequence features of the regions of 1,367,185 bp covered by 19 physically assigned P1 and TAC clones." DNA RES., 1998, pages 203-216, the whole document	1-10
A	WO 00/42205 A (NOVARTIS ERFIND VERWALT GMBH; NOVARTIS AG (CH); BUDZISZEWSKI GREGO) 20 July 2000 (2000-07-20) abstract; claims 39-44	1-10

	'
X Further documents are listed in the continuation of box C.	Patent family members are listed in annex.
 Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international filling date 	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed	involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such docu- ments, such combination being obvious to a person skilled in the art. "&" document member of the same patent family
Date of the actual completion of the international search 28 October 2003	Date of mailing of the international search report 2 0, 01, 04
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 Nt 2280 HV Rijswijk Tet. (+31-70) 340-2040, Tx. 31 651 epo nt, Fax: (+31-70) 340-3016	Authorized officer Luis Alves, D

Form PCT/ISA/210 (second sheet) (July 1992)

ERNATIONAL SEARCH REPORT

International Application No
PCT/EP 02/07929

		PCT/EP 02/0/929
C.(Continua	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	DATABASE BIOSIS [Online] BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; June 2001 (2001-06), HILLIAMS MARK A ET AL: "Characterization and inhibition of chloroplast-localized peptide deformylases from Arabidopsis thaliana" XP002253632 Database accession no. PREV200100419457 abstract & HORTSCIENCE, vol. 36, no. 3, June 2001 (2001-06), page 554, 98th Annual International Conference of the American Society for Horticultural Science; Sacramento, California, USA; July 21-25, 2001 ISSN: 0018-5345	1-10
Α	ITO TAKUYA ET AL: "Regional insertional mutagenesis of genes on Arabidopsis thaliana chromosome V using the Ac/Ds transposon in combination with a cDNA scanning method." PLANT JOURNAL, vol. 17, no. 4, February 1999 (1999-02), pages 433-444, XP002253633 ISSN: 0960-7412 the whole document	1-10
A	WO 00/15809 A (NOVARTIS ERFIND VERWALT GMBH; NOVARTIS AG (CH); BUDZISZEWSKI GREGO) 23 March 2000 (2000-03-23) abstract page 8, paragraph 3 - page 17, last paragraph	1-10

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International application No. PCT/EP 02/07929

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)
This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)
This International Searching Authority found multiple inventions in this international application, as follows:
see additional sheet
As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: See PCT/ISA/210 annex
Remark on Protest The additional search fees were accompanied by the applicant's protest. No protest accompanied the payment of additional search fees.

Form PCT/ISA/210 (continuation of first sheet (1)) (July 1998)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-10 (all partially)

Invention 1

Screening methods for herbicidal compounds comprising identifying ligands or inhibitors of the protein having SEQ Id No 2.

2. claims: 1-10 (all partially)

Inventions 2 to 48

Screening methods for herbicidal compounds comprising identifying ligands or inhibitors of the protein having SEQ Id No n (with n=4...96, n being an even number).

page 2 of 2

TERNATIONAL SEARCH REPORT

Information on patent family members

PCT/EP 02/07929

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 0042205 A	20-07-2000	AU 2290900 A CA 2362484 A1 CN 1341151 T WO 0042205 A2 EP 1141344 A2 JP 2002534128 T	01-08-2000 20-07-2000 20-03-2002 20-07-2000 10-10-2001 15-10-2002
WO 0015809 A	23-03-2000	AU 6082399 A CA 2340332 A1 CN 1318106 T WO 0015809 A2 EP 1114168 A2 JP 2002525061 T	03-04-2000 23-03-2000 17-10-2001 23-03-2000 11-07-2001 13-08-2002

Form PCT/ISA/210 (patent family annex) (July 1992)

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tct acg gcg gag gac atc gtt gat gat ctt cgt tcc agg Ser Thr Ala Glu Asp Ile Val Asp Asp Leu Arg Ser Arg 35 40 45	tac ggc aat 144 Tyr Gly Asn
ttt gcg agg ttg act cgg caa gtg ctt cta ctc aat gtc Phe Ala Arg Leu Thr Arg Gln Val Leu Leu Leu Asn Val 50 55 60	agg caa gtc 192 Arg Gln Val
ctt aat gtt aga aac aac aag agg gtt aaa gac gaa gat	gaa gat gac 24
F-	

240

Leu 65	Asn	Val	Arg	Asn	Asn 70	Lys	Arg	Val	Lys	Asp 75	Glu	Asp	Glu	As	р А . 8	o. Sp	
aac Asn	att Ile	gga Gly	gat Asp	gag Glu 85	gaa Glu	ggt Gly	tct Ser	gct Ala	tct Ser 90	cag Gln	agg Arg	aag Lys	aaa Lys	ca Gl 95	.11 -	iga Irg	288
cgg Arg	gtt Val	gat Asp	gag Glu 100	aaa Lys	gag Glu	gag Glu	aaa Lys	ttg Leu 105	cag Gln	cga Arg	gcg Ala	gag Glu	Gli Gli	1 30	g d	cat His	336
tta Leu	agg Arg	aag Lys 115	agg Arg	aat Asn	atg Met	gaa Glu	cgt Arg 120	tca Ser	gtg Val	tct Ser	tct Ser	tct Ser 125	. FI.	g to o Se	et (tct Ser	384
tct Ser	tct Ser 130	Ser	tcg Ser	gaa Glu	gac Asp	agt Ser 135	ggt Gly	gat Asp	gtg Val	tcg Ser	act Thi 140	. 56.	ga r Gl	g ga	ac sp	gcg Ala	432
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agt Ser	cta Leu	aga Arg	gat J Asp	aac Asn 165	Тут	gct Ala	aag Lys	ttg	aac Asn 170	ı sei	tc Se	c tc r Se	g aa r Ly	/S L	aa ys .75	cca Pro	528
att Ile	6 GJ? 6 G35	tcg Sei	g cct Pro) Ala	ggaa Glu	aag Lys	aat Asr	gtg Val	r GT	a gti ı Vai	t ga l Gl	g ac u Th	T A	eg a al S 90	igc Ser	aac Asn	576
aaa Lys	a ggt s Gly	aga Arg 19	g Sei	aag Lys	g ttg s Lev	g gct 1 Ala	aca Thi	. Met	g 999 t Gly	y Al	c ag a Ar	a aa g Ly 20	'S G	ag g lu <i>l</i>	gct Ala	aaa Lys	624
gtt Va:	t tc l Se: 21	r Le	t tco u Se:	c cto r Lei	c agi u Se:	gga Gly 215	z. Ala	a Th	t gg r Gl	t aa y As	t gg n G] 22	Ly As	at t sp L	tg (gaa Glu	gtt Val	672
gag Gli 22:	u Gl	t ac y Th	t aa r Ly	a gga s Gl	a cc y Pr	o Thi	ttt r Ph	t aa e Ly	a ga s As	c tt p Ph 23	e G.	gt gg ly G	gg a ly I	tt le	aag Lys	aaa Lys 240	720
at Il	a tt e Le	g ga u As	t ga p Gl	a tt u Le 24	u Gl	g at u Me	g aa t As	t gt n Va	t ct l Le 25	u Pr	c cone P	cc a ro I	tt c le I	Jeu	aat Asr 255	cct Pro	768
ga Gl	g co u Pr	g tt	t aa le Ly 26	s Ly	g at s Il	t gg e Gl	a gt y Va	g aa 1 Ly 26	rs Pr	a co o Pi	ca a	gt g er G	TA -	att [le 270	cta Lei	a ttt ı Phe	816
ca Hi	ıt gg .s G]	ja co Ly Pr 27	o Pr	t gg	ıc t <u>e</u> .y Cy	t gg s Gl	g aa y Ly 28	's TI	et aa ir Ly	ag ti ys Le	tg g eu A	ua r	at g sn :	gcc Ala	ati Il	t gcc e Ala	: 864 1
a a	sn G	aa go lu Al	et gg la Gl	gt gt Ly Va	t co	g tt to Ph	e T	r L	ag at ys I	tt t le S	er F	jcc a la 1	ca Thr	gag Glu	gt: Va	g att l Ile	912
, to	st g	gt gi	tt to	et gg	gt go	et to	t ga	aa g		at a	tc a	aga 🤉	gag	ctc	tt	t tcl	960

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ata gta aca caa ttg ttg act tgt atg gat gga cct ggt aac aaa ggc Ile Val Thr Gln Leu Leu Thr Cys Met Asp Gly Pro Gly Asn Lys Gly 355 360 365	1104
gat aaa aat gct cct gat tct agt gct ggt ttt gtt ctt gtc att gga Asp Lys Asn Ala Pro Asp Ser Ser Ala Gly Phe Val Leu Val Ile Gly 370 375	1152
gct aca aat agg cct gat gct ctt gat cct gct ttg agg aga agt gga Ala Thr Asn Arg Pro Asp Ala Leu Asp Pro Ala Leu Arg Arg Ser Gly 385 390 395 400	1200
cga ttt gaa act gag atc gct cta act gct cca gat gaa gac gca agg Arg Phe Glu Thr Glu Ile Ala Leu Thr Ala Pro Asp Glu Asp Ala Arg 405 410 415	1248
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atc ttg gat tca agg aaa tct gaa cag tct ggg gac ggt gaa gac gat Ile Leu Asp Ser Arg Lys Ser Glu Gln Ser Gly Asp Gly Glu Asp Asp 480	1440
aaa tot tgg ctg agg atg coc tgg coa gaa gaa gag ttg gaa aag cto Lys Ser Trp Leu Arg Met Pro Trp Pro Glu Glu Glu Leu Glu Lys Leu 495	1488
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tct tta aca aga gaa gga ttc tct atc gtg cct gat gtc aag tgg gat Ser Leu Thr Arg Glu Gly Phe Ser Ile Val Pro Asp Val Lys Trp Asp 515 520 525	1584
gat gtt ggt gga ctt gac cat cta cga ctt caa ttc aac cgt tat ata Asp Val Gly Gly Leu Asp His Leu Arg Leu Gln Phe Asn Arg Tyr Ile 530 535	1632
gtg agg cct atc aaa aag cct gat att tat aag gct ttt ggg gta gac	1680

Val 2	Arg	Pro	Ile	Lys	Lys 550	Pro .	Asp	Ile	Tyr :	Lys : 555	Ala :	Phe	Gly	Val	Asp 560		
tta Leu	gag Glu	aca Thr	Gly aaa	ttt Phe 565	ttg Leu	ctc Leu	tat Tyr	gga Gly	cca Pro 570	ccg Pro	ggt Gly	tgt Cys	ggc	aag Lys 575	aca Th	a r	1728
ttg Leu	att Ile	gca Ala	aag Lys 580	gca Ala	gct Ala	gct Ala	aac Asn	gag Glu 585	gct Ala	gga Gly	gct Ala	aat Asn	ttc Phe 590	atg Met	ca Hi	c . s	1776
atc Ile	aag Lys	ggt Gly 595	gcc Ala	gaa Glu	ctt Leu	cta Leu	aat Asn 600	aaa Lys	tac Tyr	gtt Val	gga Gly	gaa Glu 605	agt Ser	gag Glu	ct Le	t u	1824
gct Ala	att Ile 610	cgt Arg	acg Thr	ttg Leu	ttt Phe	cag Gln 615	cga Arg	gct Ala	cgg Arg	aca Thr	tgt Cys 620	gca Ala	cca Pro	tgt Cys	gt Va	a 1	1872
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gat Asp	ggt Gly	gga Gly	gag Glu	ı Arç	g cgt g Arg	aat Asn	gta Val	tat Tyr 665	· var	att Ile	gga Gly	gct Ala	aca Thr 670		c a	gg gg	2016
cca Pro	gat Asp	gta Va:	l Val	gat L Asp	cct Pro	gct Ala	tto Phe 680	e Let	g aga u Arg	ccg Pro	ggt Gly	aga Arg 68!	3 PIII	= gg	ga yA	at .sn	2064
ctt Lev	ctt Lev	ту:	t gta r Va.	a cco	c cto	c ccc u Pro 695) Ası	gca n Ala	a gat a As <u>ı</u>	gag Glu	g cgt 1 Arg 700	g Al	t to: a Se:	a at r Il	t c e I	ta ieu	2112
aaa Lys 705	s Ala	t at a Il	t gc e Al	a ag	g aa g Ly 71	g aaa s Ly: 0	a cc	g at	a gat e Asj	p Pro) Se.	t gt r Va	t ga l As	t ct p Le		gat Asp 720	2160
gg:	a at y Il	t gc e Al	a aa a Ly	g aa s As 72	n As	c tg n Cy	t ga s Gl	a gg u Gl	t tt y Ph 73	e se	c gg r Gl	a gc y Al	t ga a As	P DC	cc 9 eu 2 35	gca Ala	2208
ca Hi	c tt s Le	g gt u Va	g ca 1 Gl 74	n Ly	a gc s Al	t ac a Th	a tt r Ph	c ca e Gl 74	n Al	a gt a Va	g ga 1 Gl	g ga .u Gl	ıg at .u Me 75	: L I.	ta (Gly ggc	2256
tc Se	c ag r Se	r G	ng to lu Se 55	g to r Se	t ga er Gl	ia ga lu As	t ga p As 76	sp va	t ac	a ga ir As	t at p I]	'C T	eg ca nr Gl	ng to	gt ys	aca Thr	2304
at Il	c as e Ly	s Tl	eg ag nr Ai	gg ca	at ti is Pl	cc ga ne Gl	u G	aa go ln A	cc tt la Le	g to eu Se	c tter Le 78	su v	tc to	ca c er P	ca	tct Ser	2352
gt	g aa	ac a	aa ca	ag ca	aa ag	ga ag	ga ca	ac t	at ga	ac go	ca c	ta t	ca a	ca a	ag	ctt	2400

Val Asn Lys Gln Gln Arg Arg His Tyr Asp Ala Leu Ser Thr Lys Leu 785 790 795 800

Caa gaa agc gtt ggg agg aac act gaa caa gtc acc ata ggg cca tct 2448 Gln Glu Ser Val Gly Arg Asn Thr Glu Gln Val Thr Ile Gly Pro Ser 805 810 815

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Phe Ala Arg Leu Thr Arg Gln Val Leu Leu Leu Asn Val Arg Gln Val 50 55 60

Leu Asn Val Arg Asn Asn Lys Arg Val Lys Asp Glu Asp Glu Asp Asp 65 70 75 80

Asn Ile Gly Asp Glu Glu Gly Ser Ala Ser Gln Arg Lys Lys Gln Arg 85 90 95

Arg Val Asp Glu Lys Glu Glu Lys Leu Gln Arg Ala Glu Gln Ser His 100 105 110

Leu Arg Lys Arg Asn Met Glu Arg Ser Val Ser Ser Ser Pro Ser Ser 115 120 125

Ser Ser Ser Glu Asp Ser Gly Asp Val Ser Thr Ser Glu Asp Ala 130 135 140

Val Tyr Gly Glu Lys Leu Ser Pro Pro Arg Phe Asp Leu Ile Asn Asp 145 150 155 160

- Ser Leu Arg Asp Asn Tyr Ala Lys Leu Asn Ser Ser Ser Lys Lys Pro 165 170 175
- Ile Gly Ser Pro Ala Glu Lys Asn Val Glu Val Glu Thr Val Ser Asn 180 185 190
- Lys Gly Arg Ser Lys Leu Ala Thr Met Gly Ala Arg Lys Glu Ala Lys
- Val Ser Leu Ser Leu Ser Gly Ala Thr Gly Asn Gly Asp Leu Glu Val 210 215 220
- Glu Gly Thr Lys Gly Pro Thr Phe Lys Asp Phe Gly Gly Ile Lys Lys 225 230 235 240
- Ile Leu Asp Glu Leu Glu Met Asn Val Leu Phe Pro Ile Leu Asn Pro 245 250 255
- Glu Pro Phe Lys Lys Ile Gly Val Lys Pro Pro Ser Gly Ile Leu Phe 260 265 270
- His Gly Pro Pro Gly Cys Gly Lys Thr Lys Leu Ala Asn Ala Ile Ala 275 280 285
- Asn Glu Ala Gly Val Pro Phe Tyr Lys Ile Ser Ala Thr Glu Val Ile 290 295 300
- Ser Gly Val Ser Gly Ala Ser Glu Glu Asn Ile Arg Glu Leu Phe Ser 305 310 315 320
- Lys Ala Tyr Arg Thr Ala Pro Ser Ile Val Phe Ile Asp Glu Ile Asp 325 330 335
- Ala Ile Gly Ser Lys Arg Glu Asn Gln Gln Arg Glu Met Glu Lys Arg 340 345 350
- Ile Val Thr Gln Leu Leu Thr Cys Met Asp Gly Pro Gly Asn Lys Gly 355 360 365
- Asp Lys Asn Ala Pro Asp Ser Ser Ala Gly Phe Val Leu Val Ile Gly 370 375 380

Ala Thr Asn Arg Pro Asp Ala Leu Asp Pro Ala Leu Arg Arg Ser Gly 385 390 395 400

- Arg Phe Glu Thr Glu Ile Ala Leu Thr Ala Pro Asp Glu Asp Ala Arg 405 410 415
- Ala Glu Ile Leu Ser Val Val Ala Gln Lys Leu Arg Leu Glu Gly Pro
 420 425 430
- Phe Asp Lys Lys Arg Ile Ala Arg Leu Thr Pro Gly Phe Val Gly Ala 435 440 445
- Asp Leu Glu Ser Val Ala Tyr Leu Ala Gly Arg Lys Ala Ile Lys Arg 450 455
- Ile Leu Asp Ser Arg Lys Ser Glu Gln Ser Gly Asp Gly Glu Asp Asp 465 470 475 480
- Lys Ser Trp Leu Arg Met Pro Trp Pro Glu Glu Glu Leu Glu Lys Leu 485 490 495
- Phe Val Lys Met Ser Asp Phe Glu Glu Ala Val Asn Leu Val Gln Ala 500 505 510
- Ser Leu Thr Arg Glu Gly Phe Ser Ile Val Pro Asp Val Lys Trp Asp 515 520 525
- Asp Val Gly Gly Leu Asp His Leu Arg Leu Gln Phe Asn Arg Tyr Ile 530 535
- Val Arg Pro Ile Lys Lys Pro Asp Ile Tyr Lys Ala Phe Gly Val Asp 545 550 550
- Leu Glu Thr Gly Phe Leu Leu Tyr Gly Pro Pro Gly Cys Gly Lys Thr 565 570 575
- Leu Ile Ala Lys Ala Ala Ala Asn Glu Ala Gly Ala Asn Phe Met His 580 585 590
- Ile Lys Gly Ala Glu Leu Leu Asn Lys Tyr Val Gly Glu Ser Glu Leu 595 600 605
- Ala Ile Arg Thr Leu Phe Gln Arg Ala Arg Thr Cys Ala Pro Cys Val 610 615 620

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Gly Ala Trp Val Val Glu Arg Leu Leu Asn Gln Phe Leu Val Glu Leu 645 650 655

Asp Gly Glu Arg Arg Asn Val Tyr Val Ile Gly Ala Thr Asn Arg 660 665 670

Pro Asp Val Val Asp Pro Ala Phe Leu Arg Pro Gly Arg Phe Gly Asn 675 680 685

Leu Leu Tyr Val Pro Leu Pro Asn Ala Asp Glu Arg Ala Ser Ile Leu 690 695 700

Lys Ala Ile Ala Arg Lys Lys Pro Ile Asp Pro Ser Val Asp Leu Asp 705 710 715 720

Gly Ile Ala Lys Asn Asn Cys Glu Gly Phe Ser Gly Ala Asp Leu Ala 725 730 735

His Leu Val Gln Lys Ala Thr Phe Gln Ala Val Glu Glu Met Ile Gly 740 745 750

Ser Ser Glu Ser Ser Glu Asp Asp Val Thr Asp Ile Thr Gln Cys Thr 755 760 765

Ile Lys Thr Arg His Phe Glu Gln Ala Leu Ser Leu Val Ser Pro Ser 770 775 780

Val Asn Lys Gln Gln Arg Arg His Tyr Asp Ala Leu Ser Thr Lys Leu 785 790 795 800

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cga tgc ccc aaa atc ctg act tta cgc ctc gat gag aga ctc atc ccg Arg Cys Pro Lys Ile Leu Thr Leu Arg Leu Asp Glu Arg Leu Ile Pro 65 70 75 80	240
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tcc gcc att acc aaa ttt cct cca ata ctc tct cat agc gtg gag gag Ser Ala Ile Thr Lys Phe Pro Pro Ile Leu Ser His Ser Val Glu Glu 100 105 110	336
aaa ctc tgt ccc ctt ctt gct ttc ttt caa gcg tta ggt gtg cct gag Lys Leu Cys Pro Leu Leu Ala Phe Phe Gln Ala Leu Gly Val Pro Glu 115 120 125	384
act caa ctt ggc aaa atg ata ctt ttt aac cca agg ctt atc agc tac Thr Gln Leu Gly Lys Met Ile Leu Phe Asn Pro Arg Leu Ile Ser Tyr 130 135 140	432
agc atc gac acc aag ctg aca gtg atc gtc agc ttt ctt gct agc ctt Ser Ile Asp Thr Lys Leu Thr Val Ile Val Ser Phe Leu Ala Ser Leu 145 150 155 160	480
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gtc Val	atg Met 210	aat Asn	ttc Phe	cca Pro	caa Gln	ctt Leu 215	ttg Leu	tgc Cys	aga Arg	gac Asp	gtt Val 220	aac Asn	aag Lys	att Ile	ctc Leu	672
aaa Lys 225	cca Pro	aat Asn	tat Tyr	gat Asp	tat Tyr 230	ttg Leu	aag Lys	gag Glu	tgt Cys	999 Gly 235	ttt Phe	gga Gly	gat Asp	tcc Ser	cag Gln 240	720
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ttg Leu	aag Lys 290	Lys	aag Lys	gtc Val	gaa Glu	tcg Ser 295	agg Arg	ttt Phe	aaa Lys	ctt Leu	gtc Val 300	aaa Lys	aag Lys	aac Asn	aac Asn	912
att Ile 305	Asp	tgc Cys	agc Ser	ctt Leu	aga Arg 310	gaa Glu	atg Met	ctg Leu	gac Asp	tgt Cys 315	Asn	aca Thr	aag Lys	aaa Lys	ttc Phe 320	960
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<212> PRT

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Leu Glu Lys Ala Gln Ser Asp Val Ala Ser Glu Asn Trp Asp Tyr Leu 35 40 45

Ser Asn Ile Val Gly Ile Gln Glu Arg Lys Leu Pro Tyr Ile Val Ser 50 60

Arg Cys Pro Lys Ile Leu Thr Leu Arg Leu Asp Glu Arg Leu Ile Pro 65 70 75 80

Met Val Glu Cys Leu Ser Ser Leu Gly Arg Asn Pro Arg Glu Val Ala 85 90 95

Ser Ala Ile Thr Lys Phe Pro Pro Ile Leu Ser His Ser Val Glu Glu 100 105 110

Lys Leu Cys Pro Leu Leu Ala Phe Phe Gln Ala Leu Gly Val Pro Glu 115 120 125

Thr Gln Leu Gly Lys Met Ile Leu Phe Asn Pro Arg Leu Ile Ser Tyr 130 135 140

Ser Ile Asp Thr Lys Leu Thr Val Ile Val Ser Phe Leu Ala Ser Leu 145 150 155 160

Gly Leu Asp Gln Asp Gly Met Ile Gly Lys Val Leu Val Lys Asn Pro 165 170 175

Phe Leu Met Gly Tyr Ser Val Asp Lys Arg Leu Arg Pro Thr Thr Glu 180 185 190

Phe Leu Lys Ser Ser Val Gly Leu Ser Glu Asp Gly Ile Lys Ser Val 195 200 205

Val Met Asn Phe Pro Gln Leu Leu Cys Arg Asp Val Asn Lys Ile Leu 210 215 220

Lys Pro Asn Tyr Asp Tyr Leu Lys Glu Cys Gly Phe Gly Asp Ser Gln 225 230 235

Ile Ala Thr Met Val Thr Gly Tyr Pro Gln Ile Leu Ile Lys Ser Val 245 250 250

Lys Asn Ser Leu Gln Pro Arg Ile Arg Phe Leu Val Gln Val Met Gly 260 265 270

Arg Gly Met Asp Glu Val Ala Ser Tyr Pro Glu Phe Phe His His Gly 275 280 285

Leu Lys Lys Lys Val Glu Ser Arg Phe Lys Leu Val Lys Lys Asn Asn 290 295 300

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act Thr	cat His	cgc Arg	atc Ile 20	tac Tyr	aag Lys	cat His	gag Glu	tgt Cys 25	tgc Cys	atc Ile	tcc Ser	ttc Phe	gat Asp 30	act Thr	ccg Pro	!	96
aga Arg	tcc Ser	gaa Glu 35	gga Gly	gga Gly	ttg Leu	ttc Phe	gtt Val 40	gat Asp	atg Met	aat Asn	agt Ser	ttt Phe 45	ctt Leu	gct Ala	ttc Phe	1	44
G1y 999	aag Lys 50	gat Asp	tat Tyr	gtt Val	tct Ser	tgg Trp 55	aac Asn	tat Tyr	gag Glu	aag Lys	act Thr 60	gga Gly	aac Asn	cct Pro	gtt Val	1	.92
tat Tyr 65	ctt Leu	cat His	att Ile	aag Lys	cag Gln 70	act Thr	agg Arg	aag Lys	tct Ser	att Ile 75	ccc Pro	gag Glu	gat Asp	cgg Arg	cct Pro 80	2	40
ctc Leu	aag Lys	aaa Lys	ccg Pro	act Thr 85	ctg Leu	ctc Leu	gct Ala	ata Ile	ggt Gly 90	gtt Val	gat Asp	gga Gly	ggc	ttt Phe 95	gat Asp		288
aac	aat	gag	cca	gag	tac	gaq	gag	tct	tat	agc	ata	gto	ata	ctt	ccg	3	336

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gat ttt gtt Asp Phe Val	Ser Leu	Pro Phe E	ct tct gt ro Ser Va 20	I GIU Leu P	cca gag aag Pro Glu Lys 125	gtg 384 Val
agg att gct Arg Ile Ala 130	gtc gat a Val Asg	act gta of the Thr Val V	gtg aat go Wal Asn Al	cc gtt ggt g La Val Gly <i>I</i> 140	gct gag cgg Ala Glu Arg	aaa 432 Lys
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gct cgg aag Ala Arg Lys 690	gca cta a Ala Leu L	aa gcc tcg ys Ala Ser 695	gga gga ga Gly Gly As	ac att gag aaa gc sp Ile Glu Lys Al 700	a aca 2112 a Thr
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Leu Lys Lys Pro Thr Leu Leu Ala Ile Gly Val Asp Gly Gly Phe Asp 85 90 95

Asn Asn Glu Pro Glu Tyr Glu Glu Ser Tyr Ser Ile Val Ile Leu Pro 100 105 110

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- Pro Thr Leu Asp Leu Asn Met Gln Leu Thr Lys Leu Gly His Gly Leu 355 360 365
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Glu Asn Asp Met Arg Ser Ser Asp Glu Ile Val Arg Pro Arg Val Pro 500 505 510

Leu Glu Ala Cys Leu Ala Asn Phe Ala Ser Ser Glu Pro Ile Glu Asp 515 520 525

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Val Met Glu Glu Gly Trp Val Pro Lys Lys Leu Asp Val Tyr Ile Asp 565 570 575

Val Pro Asp Val Ile Asp Ile Ser His Met Arg Ser Lys Gly Leu Gln 580 585 590

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Gln Ser Ser Val Asp Thr Leu Leu Ser Phe Gly Phe Ala Glu Asp Val 675 680 685

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432

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gag Glu	att Ile	att Ile	aat Asn	cca Pro 485	gat Asp	gac Asp	tat Tyr	gtg Val	atc Ile 490	Lys	gat Asp	gaa Gli	a gad 1 Asp	ato Mei 49!	g gac : Asp	1488
cga Arg	gga Gly	gca Ala	atg Met 500	His	aac Asn	gga Gly	ggt	gat Asp 505	Val	gac	gga Gly	a agg	g cti g Lei 510	ı Asj	gag Glu	1536
gca Ala	act Thr	gct Ala 515	Ser	ctc Leu	atg Met	ctt Leu	gat Asp 520	Thr	aga Arg	cct Pro	tcg Sei	g aa r Ly 52	s Va	c at	g tcc t Ser	1584
aat Ası	gag Glu 530	ı Leı	att ı Ile	gtg Val	act	gtt Val 535	Ser	tgt Cys	tca Ser	ctt Lei	t gt ı Va 54	l Ly	a at	g ga t As	c tat p Tyr	1632
gaa Glu 54!	ı Gly	cgg Arg	g tca g Sei	a gat Asp	ggc Gly 550	Arg	tca Sei	a ato	e aag	g tc: Se: 55!	r Me	g at t Il	t gc e Al	g ca a Hi	t gtt s Val 560	1680
tc:	t cct r Pro	cta Le	a aaa u Lys	a ctt s Lev 565	ı Val	tte Lev	g gtg ı Val	g cad	g gcg s Ala 570	a Il	a gc e Al	t ga a Gl	g go u Al	t ac a Th 57	a gag r Glu 5	1728
ca ^r Hi	t ttg s Lei	g aag u Lys	g caa s Gli 580	n His	tgo Cys	tto Lei	g aad 1 Asi	c aa n Asi 58	n Ile	c tg e Cy	t co s Pr	a ca o Hi	ic gt Is Va 59	T T	t gct r Ala	1776
cc Pr	t caa o Gl	a at n Il 59	e Gl	g gaa u Gli	a acç ı Thi	g gte vai	c ga l As 60	p Va	g ac l Th	t to r Se	t ga r As	p Le	a to eu Cy 05	gt go vs A	et tac La Tyr	1824
aa	g gt	c ca	a ct	t tc	t gaa	a aa	g ct	g at	g ag	c aa	ıt gt	g a	tc tt	c a	ag aag	1872

Lys	Val 610	Gln	Leu	Ser		Lys 615	Leu	Met	Ser	Asn	Val 620	Ile	Phe	Lys		
ctg Leu 625	gga Gly	gat Asp	tca Ser	gaa Glu	gta Val 630	gct Ala	tgg Trp	gtg Val	gat Asp	tcc Ser 635	gaa Glu	gta Val	gjà aaa	aag Lys	aca Thr 640	1920
gag Glu	agg Arg	gac Asp	atg Met	agg Arg 645	tct Ser	cta Leu	cta Leu	ccg Pro	atg Met 650	cca Pro	ggt Gly	gst Ala	gct Ala	tcg Ser 655	cca Pro	1968
cac His	aaa Lys	cct Pro	gtt Val 660	cta Leu	gta Val	ggt Gly	gat Asp	ctg Leu 665	aaa Lys	atc Ile	gca Ala	gac Asp	ttc Phe 670	Lys	cag Gln	2016
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tta Leu	cgt Arg 690	Cys	ggt Gly	gaa Glu	tat Tyr	gtc Val 695	act Thr	cta Leu	cga Arg	aag Lys	gtt Val 700	gga Gly	ccg Pro	acg Thr	ggt	2112
caa Gln 705	Lys	gga Gly	gga Gly	gca Ala	tcg Ser 710	Gly	cca Pro	cag Gln	caa Gln	att Ile 715	Leu	ata Ile	gaa Glu	gga Gly	ccg Pro 720	2160
tt <u>c</u> Lev	j tgt ı Cys	gaa Glu	gac Asp	tat Tyr 725	Tyr	aaa Lys	atc Ile	agg Arg	gat Asp 730	Тут	cto Lev	tat Tyr	tct Ser	Glr 735	ttc Phe	2208
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<213> Arabidopsis thaliana

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Pro Arg Val Ala Ser Thr Ile Asp Ala Val Leu Ser His Pro Asp 50 60

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- Ser Ala Pro Val Tyr Ala Thr Glu Pro Val His Arg Leu Gly Leu Leu 85 90 95
- Thr Met Tyr Asp Gln Phe Leu Ser Arg Lys Gln Val Ser Asp Phe Asp 100 105 110
- Leu Phe Thr Leu Asp Asp Ile Asp Ser Ala Phe Gln Asn Val Ile Arg 115 120 125
- Leu Thr Tyr Ser Gln Asn Tyr His Leu Ser Gly Lys Gly Glu Gly Ile 130 135 140
- Val Ile Ala Pro His Val Ala Gly His Met Leu Gly Gly Ser Ile Trp 145 150 155 160
- Arg Ile Thr Lys Asp Gly Glu Asp Val Ile Tyr Ala Val Asp Tyr Asn 165 170 175
- His Arg Lys Glu Arg His Leu Asn Gly Thr Val Leu Gln Ser Phe Val 180 185 190
- Arg Pro Ala Val Leu Ile Thr Asp Ala Tyr His Ala Leu Tyr Thr Asn 195 200 205
- Gln Thr Ala Arg Gln Gln Arg Asp Lys Glu Phe Leu Asp Thr Ile Ser 210 215 220
- Lys His Leu Glu Val Gly Gly Asn Val Leu Leu Pro Val Asp Thr Ala 225 230 235 240
- Gly Arg Val Leu Glu Leu Leu Leu Ile Leu Glu Gln His Trp Ser Gln 245 250 255
- Arg Gly Phe Ser Phe Pro Ile Tyr Phe Leu Thr Tyr Val Ser Ser Ser 260 265 270
- Thr Ile Asp Tyr Val Lys Ser Phe Leu Glu Trp Met Ser Asp Ser Ile 275 280 285

Ser Lys Ser Phe Glu Thr Ser Arg Asp Asn Ala Phe Leu Leu Arg His 290 295 300

- Val Thr Leu Leu Ile Asn Lys Thr Asp Leu Asp Asn Ala Pro Pro Gly 305 310 315 320
- Pro Lys Val Val Leu Ala Ser Met Ala Ser Leu Glu Ala Gly Phe Ala 325 330 335
- Arg Glu Ile Phe Val Glu Trp Ala Asn Asp Pro Arg Asn Leu Val Leu 340 345 350
- Phe Thr Glu Thr Gly Gln Phe Gly Thr Leu Ala Arg Met Leu Gln Ser 355 360 365
- Ala Pro Pro Pro Lys Phe Val Lys Val Thr Met Ser Lys Arg Val Pro 370 375 380
- Leu Ala Gly Glu Glu Leu Ile Ala Tyr Glu Glu Glu Gln Asn Arg Leu 385 390 395 400
- Lys Arg Glu Glu Ala Leu Arg Ala Ser Leu Val Lys Glu Glu Glu Thr 405 410 415
- Lys Ala Ser His Gly Ser Asp Asp Asn Ser Ser Glu Pro Met Ile Ile 420 425 430
- Asp Thr Lys Thr Thr His Asp Val Val Gly Ser His Gly Pro Ala Tyr 435 440 445
- Lys Asp Ile Leu Ile Asp Gly Phe Val Pro Pro Ser Ser Ser Val Ala 450 455 460
- Pro Met Phe Pro Tyr Tyr Asp Asn Thr Ser Glu Trp Asp Asp Phe Gly 465 470 475 480
- Glu Ile Ile Asn Pro Asp Asp Tyr Val Ile Lys Asp Glu Asp Met Asp 485 490 495
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Asn Glu Leu Ile Val Thr Val Ser Cys Ser Leu Val Lys Met Asp Tyr 530 535 540

Glu Gly Arg Ser Asp Gly Arg Ser Ile Lys Ser Met Ile Ala His Val 545 550 555 560

Ser Pro Leu Lys Leu Val Leu Val His Ala Ile Ala Glu Ala Thr Glu 565 570 575

His Leu Lys Gln His Cys Leu Asn Asn Ile Cys Pro His Val Tyr Ala 580 585 590

Pro Gln Ile Glu Glu Thr Val Asp Val Thr Ser Asp Leu Cys Ala Tyr 595 600 605

Lys Val Gln Leu Ser Glu Lys Leu Met Ser Asn Val Ile Phe Lys Lys 610 615 620

Leu Gly Asp Ser Glu Val Ala Trp Val Asp Ser Glu Val Gly Lys Thr 625 630 635 640

Glu Arg Asp Met Arg Ser Leu Leu Pro Met Pro Gly Ala Ala Ser Pro 645 650 655

His Lys Pro Val Leu Val Gly Asp Leu Lys Ile Ala Asp Phe Lys Gln 660 665 670

Phe Leu Ser Ser Lys Gly Val Gln Val Glu Phe Ala Gly Gly Gly Ala 675 680 685

Leu Arg Cys Gly Glu Tyr Val Thr Leu Arg Lys Val Gly Pro Thr Gly 690 695 700

Gln Lys Gly Gly Ala Ser Gly Pro Gln Gln Ile Leu Ile Glu Gly Pro 705 710 715 720

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acc Thr	ctt Leu	ctt Leu 35	cta Leu	cga Arg	cca Pro	cta Leu	aaa Lys 40	ccg Pro	tcg Ser	gaa Glu	gtt Val	cct Pro 45	tcc Ser	ttt Phe	cgc Arg	1	144
cgg Arg	acg Thr 50	atc Ile	atc Ile	act Thr	ttc Phe	cag Gln 55	aaa Lys	att Ile	tca Ser	Thr	60 GJA 333	att Ile	gtt Val	cct Pro	cca Pro	:	192
cca Pro 65	tcg Ser	gct Ala	tca Ser	tca Ser	tct Ser 70	ccg Pro	tcg Ser	agc Ser	tat Tyr	gga Gly 75	gac Asp	ctt Leu	caa Gln	cca Pro	atc Ile 80	:	240
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gta Val	caa Gln	gag Glu	cca Pro 100	Lys	gct Ala	aaa Lys	tac Tyr	gag Glu 105	Gln	ctt Leu	atg Met	ttc Phe	tac Tyr 110	gly aaa	aag Lys		336
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cgt Arg 145	Asr	gtt Val	gtg Val	tat Tyr	gaa Glu 150	Ala	gat Asp	tct Ser	gat Asp	tcg Ser 155	· Val	cto L Lev	act 1 Thi	aaa Lys	ggg Gly 160		480
tta Leu	gct	gct Ala	cta Lev	tta Lev 165	ı Val	aag Lys	g ggt s Gly	tta Lei	tci Sei 170	c Gly	a aga Y Arg	a cct g Pro	gto Vai	l Pro	gag Glu		528

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Ser 225	Ser	Gly	gag Glu	Ser	Ser 230	Glu	Ser	Ser	Phe	Val 235	Ser	Ile	Pro	Glu	Thr 240		720
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cta Leu	gtt Val	gag Glu	gat Asp 260	ttg Leu	gga Gly	aca Thr	gaa Glu	aag Lys 265	att Ile	gat Asp	gat Asp	tct Ser	gag Glu 270	agt Ser	gjå aaa		816
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tac Tyr 305	Gln	cac His	gca Ala	gga Gly	cat His 310	gcc Ala	gct Ala	gtt Val	aga Arg	ggt Gly 315	seı Seı	gct Ala	ggt Gly	gat Asp	gat Asp 320		960
ggg Gly	gaa Glu	aca Thr	cat His	ttc Phe 325	Asn	ttg Leu	cga Arg	ato J Ile	gtt Val	. Ser	g gat : Asp	z gct o Ala	tto Phe	caa Glr 335	ggt Gly		1008
aa <i>a</i> Lys	ago Ser	ttg Leu	gtc Val 340	Lys	aga Arg	cat His	agg Arg	g ctg g Lev 345	ı Ile	a tat e Tyi	gae As	c ttg p Lêv	tto Lev 350	1 GT1	a gat n Asp		1056
gaç Glu	g ttg Lev	aag Lys 355	Ser	. Gly	tta Leu	cat His	gct Ala 360	a Let	tci Sei	t ati	t gte	g gca 1 Ala 36	а Гу	g act	t cct r Pro		1104
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Arg Thr Ile Ile Thr Phe Gln Lys Ile Ser Thr Gly Ile Val Pro Pro 50 55 60

Pro Ser Ala Ser Ser Ser Pro Ser Ser Tyr Gly Asp Leu Gln Pro Ile
65 70 75 80

Glu Glu Leu Pro Pro Lys Leu Gln Glu Ile Val Lys Leu Phe Gln Ser 85 90 95

Val Gln Glu Pro Lys Ala Lys Tyr Glu Gln Leu Met Phe Tyr Gly Lys 100 105 110

Asn Leu Thr Pro Leu Asp Ser Gln Phe Lys Thr Arg Glu Asn Lys Val

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Arg Asn Val Val Tyr Glu Ala Asp Ser Asp Ser Val Leu Thr Lys Gly 145 150 155 160

Leu Ala Ala Leu Leu Val Lys Gly Leu Ser Gly Arg Pro Val Pro Glu 165 170 175

Ile Leu Arg Ile Thr Pro Asp Phe Ala Val Leu Leu Gly Leu Gln Gln 180 185 190

Ser Leu Ser Pro Ser Arg Asn Asn Gly Leu Leu Asn Met Leu Lys Leu 195 200 205

Met Gln Lys Lys Ala Leu His Leu Glu Val Lys Gly Glu Glu Asp Ser 210 215 220

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Lys Asp Glu Ala Asn Val Pro Glu Val Asp Leu Glu Ser Lys Pro Asp 245 250 255

Leu Val Glu Asp Leu Gly Thr Glu Lys Ile Asp Asp Ser Glu Ser Gly 260 265 270

Ser Asn Val Val Ala Leu Gly Ser Arg Gly Met Arg Ile Arg Glu Lys 275 280 285

Leu Glu Lys Glu Leu Asp Pro Val Glu Leu Glu Val Glu Asp Val Ser 290 295 300

Tyr Gln His Ala Gly His Ala Ala Val Arg Gly Ser Ala Gly Asp Asp 305 310 315 320

Gly Glu Thr His Phe Asn Leu Arg Ile Val Ser Asp Ala Phe Gln Gly 325 330 335

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tct Ser	cac His	gcc Ala 35	gac Asp	ggt Gly	gtt Val	tca Ser	ccg Pro 40	att Ile	ctt Leu	gct Ala	tct Ser	tgc Cys 45	agt Ser	ggc	gat Asp	144
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tct Ser	ggt Gly 130	Ser	tgc Cys	ctt Leu	gca Ala	aca Thr	Cys	agt Ser	aga Arg	gat JASP	: aag : Lys 140	s Sei	gti Val	t tgg l Trj	g att p Ile	432
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ga: Gl:	a gat u As	t gai p Asj 19!	g Ası	t ggt o Gl	t gag y Gl	g tai u Ty:	ca r Gl:	n Cy	t gto	c ca l Gl	a ac n Th	c tt r Le 20	u Gl	gt ga .y Gl	a tct u Ser	624
aa As:	c aa n As: 21	n Gl	t cad	c tc	t tc r Se	a acgrant	r Va	a tg 1 Tr	g tc p Se	c at r Il	c to e Se 22	r Ph	t aa ie As	ac go sn Al	t gca .a Ala	672 a
aa	a aa	c aa	g at	g gt	c ac	t tg	t ag	t ga	t ga	t ct	a ac	c tt	g aa	ag at	a tgg	720

Gly 225	Asp	Lys	Met	Val	Thr 230	Cys	Ser	Asp	Asp	Leu 235	Thr	Leu	Lys	Ile	Trp 240	
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Ser His Ala Asp Gly Val Ser Pro Ile Leu Ala Ser Cys Ser Gly Asp 35 40 45

Asn Thr Val Arg Ile Trp Glu Gln Ser Ser Leu Ser Arg Ser Trp Thr 50 55 60

Cys Lys Thr Val Leu Glu Glu Thr His Thr Arg Thr Val Arg Ser Cys 65 70 75 80

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- Thr Thr Gly Ile Trp Lys Asn Tyr Gly Ser Glu Phe Glu Cys Ile Ser
- Thr Leu Glu Gly His Glu Asn Glu Val Lys Ser Val Ser Trp Asn Ala 115 120 125
- Ser Gly Ser Cys Leu Ala Thr Cys Ser Arg Asp Lys Ser Val Trp Ile 130 135 140
- Trp Glu Val Leu Glu Gly Asn Glu Tyr Asp Cys Ala Ala Val Leu Thr 145 150 155 160
- Gly His Thr Gln Asp Val Lys Met Val Gln Trp His Pro Thr Met Asp 165 170 175
- Val Leu Phe Ser Cys Ser Tyr Asp Asn Thr Ile Lys Val Trp Trp Ser 180 185 190
- Glu Asp Asp Gly Glu Tyr Gln Cys Val Gln Thr Leu Gly Glu Ser 195 200 205
- Asn Asn Gly His Ser Ser Thr Val Trp Ser Ile Ser Phe Asn Ala Ala 210 215 220
- Gly Asp Lys Met Val Thr Cys Ser Asp Asp Leu Thr Leu Lys Ile Trp 225 230 235 240
- Gly Thr Asp Ile Ala Lys Met Gln Ser Gly Glu Glu Tyr Ala Pro Trp 245 250 255
- Ile His Leu Cys Thr Leu Ser Gly Tyr His Asp Arg Thr Ile Tyr Ser 260 265 270
- Ala His Trp Ser Arg Asp Asp Ile Ile Ala Ser Gly Ala Gly Asp Asn 275 280 285
- Ala Ile Arg Leu Phe Val Asp Ser Lys His Asp Ser Val Asp Gly Pro 290 295 300

Ser Tyr Asn Leu Leu Lys Lys Asn Lys Ala His Glu Asn Asp Val 310 Asn Ser Val Gln Trp Ser Pro Gly Glu Gly Asn Arg Leu Leu Ala Ser 330 Ala Ser Asp Asp Gly Met Val Lys Ile Trp Gln Leu Ala Thr Lys Pro 345 <210> 39 <211> 942 <212> DNA <213> Arabidopsis thaliana <220> CDS <221> (1)..(924) <222> <223> <400> 39 atg cta agc ttg aga tat tca tta cct tat ctt ctt caa aca agg 48 Met Leu Ser Leu Arg Tyr Ser Leu Pro Tyr Leu Leu Gln Thr Arg 5 gaa tca tca act aag ctc ttc acc aaa aag cct aac aat gtt gtg gtt 96 Glu Ser Ser Thr Lys Leu Phe Thr Lys Lys Pro Asn Asn Val Val Val tgt gcg gcg aga ggt cca aga cct cgg tct cct cgt gta tgg aaa aca 144 Cys Ala Ala Arg Gly Pro Arg Pro Arg Ser Pro Arg Val Trp Lys Thr 35 192 agg aag agg att gga act atc tct aaa gct gcc aaa atg att gct tgt Arg Lys Arg Ile Gly Thr Ile Ser Lys Ala Ala Lys Met Ile Ala Cys 50 ata aaa gga ttg tcg aat gtt aaa gaa gaa gtt tat gga gcg ctt gat 240 Ile Lys Gly Leu Ser Asn Val Lys Glu Glu Val Tyr Gly Ala Leu Asp 70 tcc ttc att gct tgg gaa tta gag ttc cct ctt gtt ata gtt aag aag 288 Ser Phe Ile Ala Trp Glu Leu Glu Phe Pro Leu Val Ile Val Lys Lys 85 90 336 Ala Leu Val Ile Leu Glu Asp Glu Lys Glu Trp Lys Lys Ile Ile Gln

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gtg Val	aaa Lys	ccg Pro 195	Asn	gtt Val	gcg Ala	att Ile	gtg Val 200	Ser	atg Met	gtt Val	gga Gly	aaa Lys 205	vaı	ttt Phe	gtg Val	<b>624</b> _.
aaa Lys	cta Leu 210	Glu	atg Met	aag Lys	gat Asp	aag Lys 215	Tyr	gag Glu	aaa Lys	ctg Leu	atg Met 220	: гАз	aaa Lys	tat Tyr	cct Pro	672
cca Pro 225	cca Pro	cag Gln	tgg Trp	gag Glu	ttt Phe 230	Arg	tac	atc : Ile	aaa Lys	gga Gly 235	Arc	a cgt g Arg	gtt Ual	aag Lys	g gtc Val 240	720
aag Lys	gca Ala	aag Lys	cag Gln	ctg Leu 245	Asn	gag Glu	cta Lev	ago Ser	gaa Glu 250	r GTZ	gaa Glu	a ggt ı Gl	ggt Gly	tta / Let 25!	a agc ı Ser	768
agc Ser	gac Asp	gaa Glu	gat Asp 260	Lys	att Ile	gac Asp	aat Ası	gag Glu 265	ı Ile	gag Glu	g agt u Se:	t gaa	a gaa u Gli 270	1 GT	a gat u Asp	816
ggt Gly	gag	gat Asp 275	Lev	agt Ser	gaa Glu	a gaq a Glu	g gaa 1 Gl: 28	ı Glı	a gat ı Ası	ga: o Gl	a aa u Ly	a ga s Gl 28	и ье	t tt u Le	g ggt u Gly	864
gga Gly	agt Sei 290	Gli	a gga n Gly	cag Glr	g att 1 Ile	act Thi	r Se	t aga	a ga g Gl	a cc u Pr	c ag o Se 30	r Le	t ga u As	t ca p Hi	t ttg s Leu	912
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Ala Leu Val Ile Leu Glu Asp Glu Lys Glu Trp Lys Lys Ile Ile Gln
100 105 110

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Tyr Phe Ser Leu Leu Asn Ala Leu Ala Glu Asp Asn Arg Leu Asp Glu 130 135 140

Ala Glu Glu Leu Trp Asn Lys Leu Phe Met Glu His Leu Glu Gly Thr 145 150 155 160

Pro Arg Lys Phe Phe Asn Lys Met Ile Ser Ile Tyr Tyr Lys Arg Asp 165 170 175

Met His Gln Lys Leu Phe Glu Val Phe Ala Asp Met Glu Glu Leu Gly 180 185

Val Lys Pro Asn Val Ala Ile Val Ser Met Val Gly Lys Val Phe Val 195 200 205

Lys Leu Glu Met Lys Asp Lys Tyr Glu Lys Leu Met Lys Lys Tyr Pro 215 Pro Pro Gln Trp Glu Phe Arg Tyr Ile Lys Gly Arg Arg Val Lys Val 230 Lys Ala Lys Gln Leu Asn Glu Leu Ser Glu Gly Glu Gly Leu Ser 250 245 Ser Asp Glu Asp Lys Ile Asp Asn Glu Ile Glu Ser Glu Glu Glu Asp 265 Gly Glu Asp Leu Ser Glu Glu Glu Glu Asp Glu Lys Glu Leu Leu Gly 285 280 275 Gly Ser Gln Gly Gln Ile Thr Ser Arg Glu Pro Ser Leu Asp His Leu 300 295 290 Asp Ser Ser 305 <210> 41 <211> 2427 <212> DNA <213> Arabidopsis thaliana <220> <221> CDS <222> (1)..(2427) <223> 21878 <400> 41 atg gta aag gaa act cta att cct ccg tca tct acg tca atg acg acc 48 Met Val Lys Glu Thr Leu Ile Pro Pro Ser Ser Thr Ser Met Thr Thr gga aca tet tet tet teg tet ett tea atg acg tta tee tea aca aac 96 Gly Thr Ser Ser Ser Ser Leu Ser Met Thr Leu Ser Ser Thr Asn 144 gcg tta tcg ttt ttg tcg aaa gga tgg aga gag gta tgg gat tca gca Ala Leu Ser Phe Leu Ser Lys Gly Trp Arg Glu Val Trp Asp Ser Ala

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cta Leu 65	gca Ala	tca Ser	acg Thr	ttc Phe	gat Asp 70	aga Arg	gag Glu	atc Ile	gag Glu	aat Asn 75	ttc Phe	ctc Leu	aat Asn	aac Asn	se 80	-	240
gcg Ala	agg Arg	tct Ser	gcg Ala	ttt Phe 85	ccc Pro	gtt Val	ggt Gly	tca Ser	cca Pro 90	tcg Ser	gcg	tcg Ser	tct Ser	ttc Phe 95	to Se	a er	288
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cgt Arg	agg Arg	gtt Val 115	Tyr	tcg Ser	gcg Ala	ccg Pro	gag Glu 120	тте	agt Ser	cgc Arg	aag J Lys	g gtt s Val 129	1100	gag Glu	ag 1 Al	ga rg	384
tgg Trp	gga Gly 130	Pro	gcg Ala	aga Arg	gcg Ala	aag Lys 135	ctt Leu	gga	a ato / Met	g gat . Asj	cta b Le	u DC	g gcg r Ala	g att a Ile	e L	ys	432
aag Lys 145	: Ala	g att	gtç Val	tct Ser	gag Glu 150	Met	gaa Glu	tto Lei	g gat u Asj	t ga p Gl [*] 15	u Al	t ca g Gl	g ggg n Gl	a gt y Va		tg eu .60	480
gag Glu	ato 1 Mei	g agt E Sei	t aga r Arg	ttg J Lev 165	ı Arg	aga Arg	cgg J Arg	g cg	t aa g As 17	n se	t ga r As	t ag p Ar	g gt g Va	t ag l Ar 17	9 -	tt he	528
acç Thi	g gag r Gl	g tt u Ph	t tte e Phe 18	c gcg e Ala	g gag a Glu	g gct L Ala	gag a Gl	g ag u Ar 18	g As	t gg p Gl	ga ga .y Gl	a go lu Al	t ta a Ty 19		c c	ggt 3ly	576
ga As	t tg p Tr	g ga p Gl 19	u Pr	g att	t agg	g tci g Se:	t tt r Le 20	u Ly	ıg aç rs Se	gt ag er Al	ga ti cg Pl	re ri	aa ga ys Gl OS	ig tt Lu Pl	t g	gag Glu	624
aa Ly	a cg s Ar 21	g Se	c to r Se	g tt r Le	a ga u Gl	a at u Il 21	е ге	g aç u Se	gt gg er G	ga ti Ly Pl	ue n	ag a ys A 20	ac ag sn Se	gt ga er G	aa lu	ttt Phe	672
gt Va 22	1 G]	ıg aa Lu Ly	ıg ct /s Le	c aa u Ly	a ac s Th 23	r Se	c tt r Ph	t aa le Ly	aa to ys S	er 1	tt t le T 35	ac a 'yr L	aa g ys G	aa a lu T	ct hr	gat Asp 240	720
ga G1	ig go	ct aa la Ly	ag ga ys As	it gt sp Va 24	l Pr	t co o Pr	g ti	eu A	sp v	ta c al P 50	ct g ro G	gaa c Blu I	tg t eu L	Cu z	ca la !55	tgt Cys	768
t t Le	eu V	tt ag al A	rg G	aa to In Se	t ga er Gl	a co .u Pi	t ti	he L	tt g eu A 65	at c sp G	ag a ln l	att g	TA A	tt a al <i>P</i> 70	aga Arg	aag Lys	816
9° A:	at a sp T	ca t hr C	gt g ys A	ac co	ga at cg II	a gt Le Va	al G	aa a lu S	gc c Ser I	ett t Leu (	gc a	aaa ( Lys (	cgc a	aag a	agc Ser	caa Gln	864

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gat Asp 305	aac Asn	cat His	gga Gly	gtt Val	gat Asp 310	ttg Leu	gat Asp	atg Met	agg Arg	ata Ile 315	gcc Ala	agt Ser	gtt Val	ctt Leu	caa Gln 320	960
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tgg Trp 385	Leu	tgc Cys	gaa Glu	tct Ser	gat Asp 390	caa Gln	gaa Glu	cta Leu	gtg Val	tat Tyr 395	Pro	aac Asn	aat Asn	cto Lev	acc Thr 400	1200
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gaa Glu	agg Arg	g att g Ile	ggt Gly 420	Phe	aag Lys	gct Ala	gat Asp	ttt Phe 425	. Lys	ato ; Ile	c tco e Sei	ttt Phe	tac Tyr 430	Pro	a gga o Gly	1296
aag Lys	g ttt s Phe	tca Ser 435	. Lys	gaa Glu	agg Arg	cgc Arg	ago Ser 440	· Ile	ttt Phe	cct Pro	t gct	t ggt a Gly 44!	y Asj	c act	t tct r Ser	1344
caa Gl:	a tti n Phe 450	e Ile	a tog e Sei	tca Ser	aaa Lys	gat Asp 455	Ala	gad Asp	e att	e Ala	t at a Il 46	е те	t gaa u Gl	a ga u Gl	a cct u Pro	1392
ga: Gl: 46	u Hi	t cto s Leo	c aad u Ası	e tgg n Trp	tato Tyr 470	тут	cac His	e ggo s Gly	c aag y Lys	g cg s Ar 47	g Tr	g ac p Th	t ga r As	t aa p Ly	a ttc s Phe 480	1440
aa As	c ca n Hi	t gt s Va	t gt 1 Va	t gga 1 Gl ₃ 48!	/ Ile	gto Val	c cad	c ac	a aa r As 49	n Ty	c tt r Le	a ga u Gl	g ta u Ty	c at r Il 49	c aag e Lys 5	1488
ag Ar	g ga g Gl	g aa u Ly	g aa s As: 50	n Gl	a gct y Ala	cti a Lei	ca ıGl	a gc n Al 50	a Ph	t tt e Ph	t gt ie Va	g aa 11 As	c ca n Hi 51	S Va	a aac il Asn	1536
aa As	t tg n Tr	g gt p Va	c ac l Th	a cg	a gcg g Ala	g tai	t tg r Cy	t ga s As	c aa p Ly	g gt	t ct	eu Ar	g Le	c to	et gcg er Ala	1584

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525 520 515

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Asn Pro Lys Phe Leu Met Ile	Gly Glu Lys Ile Ala	Glu Glu Arg Ser	
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Lys Ser Glu Leu Gly Ser Pho	e Asn Leu Asp Val Tyi	Gly Asn Gly Glu	
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Ala Glu Ala Leu Ala Met G	ly Lys Phe Val Val C	ys Ala Asp His Pro	
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Ser Asn Glu Phe Phe Arg S	er Phe Pro Asn Cys L	eu Thr Tyr Lys Thr	
675	680	685	
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Leu Pro Leu Thr Pro Glu (	Gln Met Tyr Asn Leu S	Ser Trp Glu Ala Ala	
705 710	715	720	
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gga gag gga gga agg aag Gly Glu Gly Gly Arg Lys 740	745	750	2256
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Asn Glu Val Val Asp Gly	Gly Leu Ala Phe Ser	His Tyr Val Leu Thr	

755 760 765

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Ala Arg Ser Ala Phe Pro Val Gly Ser Pro Ser Ala Ser Ser Phe Ser 85 90 95

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Lys Arg Ser Ser Leu Glu Ile Leu Ser Gly Phe Lys Asn Ser Glu Phe 210 215

Val Glu Lys Leu Lys Thr Ser Phe Lys Ser Ile Tyr Lys Glu Thr Asp 225 230 235 240

Glu Ala Lys Asp Val Pro Pro Leu Asp Val Pro Glu Leu Leu Ala Cys 245 250 . 255

Leu Val Arg Gln Ser Glu Pro Phe Leu Asp Gln Ile Gly Val Arg Lys 260 265 270

Asp Thr Cys Asp Arg Ile Val Glu Ser Leu Cys Lys Cys Lys Ser Gln 275 280 285

Gln Leu Trp Arg Leu Pro Ser Ala Gln Ala Ser Asp Leu Ile Glu Asn 290 295 300

Asp Asn His Gly Val Asp Leu Asp Met Arg Ile Ala Ser Val Leu Gln 305 310 315

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Pro Glu Thr Pro Glu Asn Lys Arg His Val Ala Ile Val Thr Thr Ala 340 345

Ser Leu Pro Trp Met Thr Gly Thr Ala Val Asn Pro Leu Phe Arg Ala 355 360 365

Ala Tyr Leu Ala Lys Ala Lys Gln Ser Val Thr Leu Val Val Pro

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Trp Leu Cys Glu Ser Asp Gln Glu Leu Val Tyr Pro Asn Asn Leu Thr 

Phe Ser Ser Pro Glu Glu Glu Ser Tyr Ile Arg Lys Trp Leu Glu 

Glu Arg Ile Gly Phe Lys Ala Asp Phe Lys Ile Ser Phe Tyr Pro Gly 

Lys Phe Ser Lys Glu Arg Arg Ser Ile Phe Pro Ala Gly Asp Thr Ser 

Gln Phe Ile Ser Ser Lys Asp Ala Asp Ile Ala Ile Leu Glu Pro 

Glu His Leu Asn Trp Tyr Tyr His Gly Lys Arg Trp Thr Asp Lys Phe 

Asn His Val Val Gly Ile Val His Thr Asn Tyr Leu Glu Tyr Ile Lys 

Arg Glu Lys Asn Gly Ala Leu Gln Ala Phe Phe Val Asn His Val Asn

Asn Trp Val Thr Arg Ala Tyr Cys Asp Lys Val Leu Arg Leu Ser Ala . 520

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Asn Pro Lys Phe Leu Met Ile Gly Glu Lys Ile Ala Glu Glu Arg Ser 

Arg Gly Glu Gln Ala Phe Ser Lys Gly Ala Tyr Phe Leu Gly Lys Met 

Val Trp Ala Lys Gly Tyr Arg Glu Leu Ile Asp Leu Met Ala Lys His 

Lys Ser Glu Leu Gly Ser Phe Asn Leu Asp Val Tyr Gly Asn Gly Glu 

Asp Ala Val Glu Val Gln Arg Ala Lys Lys His Asp Leu Asn Leu

610 615 620

Asn Phe Leu Lys Gly Arg Asp His Ala Asp Asp Ala Leu His Lys Tyr 625 630 635 640

Lys Val Phe Ile Asn Pro Ser Ile Ser Asp Val Leu Cys Thr Ala Thr 645 650 655

Ala Glu Ala Leu Ala Met Gly Lys Phe Val Val Cys Ala Asp His Pro 660 665 670

Ser Asn Glu Phe Phe Arg Ser Phe Pro Asn Cys Leu Thr Tyr Lys Thr 675 680 685

Ser Glu Asp Phe Val Ser Lys Val Gln Glu Ala Met Thr Lys Glu Pro 690 695 700

Leu Pro Leu Thr Pro Glu Gln Met Tyr Asn Leu Ser Trp Glu Ala Ala 705 710 715 720

Thr Gln Arg Phe Met Glu Tyr Ser Asp Leu Asp Lys Ile Leu Asn Asn 725 730 735

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Gly Asn Asp Phe Leu Arg Leu Cys Thr Gly Ala Thr Pro Arg Thr Lys
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Pro	aag Lys 210	aaa Lys	ggt Gly	act Thr	tgc Cys	atg Met 215	tac Tyr	agg Arg	aga Arg	aga Arg	gaa Glu 220	т ге	g g u A	ca a la '	act Thr	tc. Se	a r	672
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ga G1	ag ad lu Tì	ca to nr So	er L	aa ti ys Pl 20	tc to	gc to ys Se	ca ga er G	lu C	gt g ys G 25	gt t	cc Ser	aag Lys	aga Arg	a ct g Le 43	:u G	Jy gg	ata Ile	1296

1299 tag .

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<213> Arabidopsis thaliana

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Ser Leu Asp Asn Asp Gly Asp Ser Ser Ser Ala Asp Cys Met His Glu 50 55 60

Ser Tyr Arg Asn Ser Met Gln Ile Gly Val Glu Glu Gly Gly Ser Asn 70 75 80

Met Glu Asn Lys Gly Ser Ala Tyr Ile Met Leu Asn Ile Glu Asp Val 85 90 95

Ser Pro Ile Glu Ala Ala Arg Gly Arg Phe Leu Gln Ile Ile Leu Asp 100 105 110

Tyr Phe Ile Ser Gln His Val Ile Glu Val Cys Glu Ser Lys Arg Asp 115 120 125

His Asp Val Asp Ser Gly Gly Arg Asp Ser Asn Ser Lys Val Lys Arg 130 135 140

Lys Ser Asp Asp Thr Arg Tyr Glu Gly Asp Pro Ser Phe Ala Leu Pro 145 150 155 160

Leu Met Tyr Ile Ala Asn Leu Tyr Glu Thr Leu Val Gly Glu Ala Asn 165 170 175

Val Arg Leu Ala Ser Leu Asn Gly Ile Arg Asp Lys Thr Ile Gly Val 180 185 190

Ala Leu Glu Ala Ala Gly Gly Leu Tyr Arg Lys Leu Thr Lys Lys Phe 195 200 205

Pro Lys Lys Gly Thr Cys Met Tyr Arg Arg Glu Leu Ala Thr Ser 210 215 220

Val Glu Thr Arg Thr Arg Phe Pro Glu Leu Val Ile His Glu Glu Lys 225 230 235 240

Arg Val Arg Phe Val Val Val Asn Gly Leu Asp Ile Val Glu Lys Pro 245 250 255

Ser Asp Leu Pro Ile Glu Glu Ala Glu Trp Phe Lys Arg Leu Thr Gly 260 265 270

Arg Asn Glu Val Ala Ile Ser Ala Arg Asp Tyr Lys Phe Tyr Cys Pro 275 280 285

Arg Arg Lys His Arg Arg Leu Gln Asn Ser Val Ser Ser Ile Asn Gly
290 295 300

Leu Pro Thr Phe Pro Gly Ile Asp Ser Ser Thr Leu Ala Asn Thr Gln 305 310 315 320

Gly Phe Arg Glu Asp Gln Ser Gln Gln Gln His Thr Pro Ser Pro Ser 325 330 335

Lys His His Met Ser Ser Leu Ser His Gln Phe His Gln Ser Ile His 340 345 350

Gln Ser His Gln His His Gln Ser Ile Tyr Gln Ser Gln His Ala Ala 355 360 365

Thr His Tyr Pro Ser Gln Asn His Gln Cys Asp Pro Glu Leu Ser His 370 375 380

Thr Gln Met Ala Cys Leu Gln Pro Leu Thr Gly Gly His Val Met Pro 385 390 395 400

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aat Asn	agc Ser	atg Met	tat Tyr 20	tta Leu	cgt Arg	gag Glu	acc Thr	ata Ile 25	ctt Leu	tct Ser	agt Ser	gaa Glu	tct Ser 30	cct Pro	agt Ser	. 96	;
ctc Leu	aac Asn	act Thr 35	cag Gln	aat Asn	atc Ile	tca Ser	gtg Val 40	aca Thr	gtt Val	gaa Glu	atg Met	cca Pro 45	ccc Pro	atg Met	ttg Leu	144	1
aaa Lys	ccg Pro 50	ttg Leu	cat His	gly aaa	cat His	ctt Leu 55	ctt Leu	aaa Lys	cac His	ttt Phe	att Ile 60	gtg Val	ttt Phe	tca Ser	aat Asn	19	2
att Ile 65	gaa Glu	gac Asp	cag Gln	aac Asn	agt Ser 70	atc Ile	atc Ile	ata Ile	ata Ile	att Ile 75	cat His	gct Ala	act Thr	aac Asn	aat Asn 80	24	0
tgt Cys	cta Leu	cag Gln	cgt Arg	tgc Cys 85	ccg Pro	tca Ser	gtt Val	act Thr	aaa Lys 90	gaa Glu	cag Gln	tgg Trp	gca Ala	gtg Val 95	cca Pro	28	8
gcg	att Ile	ttg Leu	tct Ser 100	Ser	ttg Leu	aaa Lys	atg Met	gaa Glu 105	GIU	aac Asr	ctt Leu	ttg Lev	gco Ala 110	, GIL	gaa Glu	33	16
agg Arg	g gco g Ala	tgt Cys	: Val	g tto L Phe	ctc Leu	tcc Ser	tto Lev	ı Lev	ı ctg Leu	cat His	aac Asr	tto Phe 125	: 56	c ato r Met	gtt Val	38	34
cad	aca	a aca	a aaa	a act	. ggg	g aat v Ast	act Thi	c cto	g aat 1 Asr	gti Va	t gat l Asp	t tot	t tte	c tco e Sei	tgc Cys	. 4:	32

135

140

130

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gct gga gtt atg ctt tct gga ttt tcg gaa gaa ctc ctt tgt ctt ctt Ala Gly Val Met Leu Ser Gly Phe Ser Glu Glu Leu Leu Cys Leu Leu 165	528
cag gac ctc ctt tct ggg cag cgg gta tta ttt tcg gtt aaa tcc tca Gln Asp Leu Leu Ser Gly Gln Arg Val Leu Phe Ser Val Lys Ser Ser 180 185	576
gaa aca tgt gaa tct gat tta agc atc cct gtc acc ctg aat gga gaa Glu Thr Cys Glu Ser Asp Leu Ser Ile Pro Val Thr Leu Asn Gly Glu 195 200 205	624
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gga agc gct att ttg gcg gca ata tgt act gca ctt gat cgt att gga Gly Ser Ala Ile Leu Ala Ala Ile Cys Thr Ala Leu Asp Arg Ile Gly 225 230 235	720
tat atc tgc gaa gct tcc ttt gaa atc ctg cac aag tac agt cat gag Tyr Ile Cys Glu Ala Ser Phe Glu Ile Leu His Lys Tyr Ser His Glu 245 250 255	768
aaa acc tca gtg cta ctg acc att ctt cac gtt ttt gct tac att gct Lys Thr Ser Val Leu Leu Thr Ile Leu His Val Phe Ala Tyr Ile Ala 260 265 270	816
gga gag aaa atg gtg ttg tct agt gag cat ggc ata tca att gca gtg Gly Glu Lys Met Val Leu Ser Ser Glu His Gly Ile Ser Ile Ala Val 275 280 285	864
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gac agg tct tcc tcg ctg gag gct atg gca tct aag ctc atg gaa att Asp Arg Ser Ser Ser Leu Glu Ala Met Ala Ser Lys Leu Met Glu Ile 325 330 335	1008
ctt cag gaa ttt act gag tct aat act ttg cat aaa agc ttg act ggt Leu Gln Glu Phe Thr Glu Ser Asn Thr Leu His Lys Ser Leu Thr Gly 340 345	1056
tca ttg ggt tct agc cac cta gag aag acc gag ttt agg ccg gca cac Ser Leu Gly Ser Ser His Leu Glu Lys Thr Glu Phe Arg Pro Ala His 355 360 365	1104
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1	cca Pro	ttg Leu	cca Pro	atg Met 420	aac Asn	ctc Leu	tct Ser	gtt Val	gca Ala 425	atc Ile	gtc Val	tcc Ser	ctt Leu	ctt Leu 430	gjà aaa	caa Gln	1296
1	ctt Leu	agc Ser	agt Ser 435	att Ile	gga Gly	gtg Val	gat Asp	gct Ala 440	ggt Gly	ggc	tat Tyr	gaa Glu	aac Asn 445	Gra	gga Gly	atc Ile	1344
	tca Ser	aac Asn 450	ttg Leu	aga Arg	gtg Val	aaa Lys	ctg Leu 455	tca Ser	gca Ala	ttt Phe	cta Leu	cag Gln 460	tgt Cys	gag Glu	acg Thr	aca Thr	1392
	cta Leu 465	Lys	gcc Ala	ggt Gly	ttt Phe	gca Ala 470	Val	cag Gln	ata Ile	gca	act Thr 475	Val	agc Ser	tcc	ctc Leu	Leu 480	1440
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	atg Met	att Ile	ccg Pro	ggt Gly 500	ser Ser	gly	gac Asp	caa Glr	ago Ser 505	Lev	a tct 1 Ser	ggt Gly	tca Sei	yto Val	LASI	gtg 1 Val	1536
	gto Val	aco Thr	aag Lys 515	Tr	tto Lev	g tog 1 Ser	tto Lev	tto Leu 520	ı Sei	c aag	g gaa s Glu	a caa 1 Gli	a cga n Arg 529	g va.	t tto l Pho	c gca e Ala	1584
	ttt Phe	gag Glu 530	ı Phe	t cta e Lei	a caa ı Glı	a aco	aat Ası 53!	ı Val	gt: L Va	t aga	a tga g	<b>a</b>					1617

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Leu Asn Thr Gln Asn Ile Ser Val Thr Val Glu Met Pro Pro Met Leu 35 40 45

- Lys Pro Leu His Gly His Leu Leu Lys His Phe Ile Val Phe Ser Asn 50 60
- Ile Glu Asp Gln Asn Ser Ile Ile Ile Ile Ile His Ala Thr Asn Asn 65 70 75 80
- Cys Leu Gln Arg Cys Pro Ser Val Thr Lys Glu Gln Trp Ala Val Pro 85 90 95
- Ala Ile Leu Ser Ser Leu Lys Met Glu Glu Asn Leu Leu Ala Gln Glu
  100 105 110
- Arg Ala Cys Val Phe Leu Ser Leu Leu Leu His Asn Phe Ser Met Val
- His Thr Thr Lys Thr Gly Asn Thr Leu Asn Val Asp Ser Phe Ser Cys 130
- Leu Asp Ser Phe Ser Lys His Ile Arg Gly Gly Met Ala Asp Thr Glu 145 150 155 160
- Ala Gly Val Met Leu Ser Gly Phe Ser Glu Glu Leu Leu Cys Leu Leu 175
- Gln Asp Leu Leu Ser Gly Gln Arg Val Leu Phe Ser Val Lys Ser Ser 180 185 190
- Glu Thr Cys Glu Ser Asp Leu Ser Ile Pro Val Thr Leu Asn Gly Glu 195 200 205
- Asn Val Ala Leu Val Asn Lys Ile Ala Leu Thr Asp Gln Leu Val Ala 210 215 220
- Gly Ser Ala Ile Leu Ala Ala Ile Cys Thr Ala Leu Asp Arg Ile Gly 225 230 235 240
- Tyr Ile Cys Glu Ala Ser Phe Glu Ile Leu His Lys Tyr Ser His Glu 245 250 255
- Lys Thr Ser Val Leu Leu Thr Ile Leu His Val Phe Ala Tyr Ile Ala 260 265 270

Gly Glu Lys Met Val Leu Ser Ser Glu His Gly Ile Ser Ile Ala Val 275 280 285

- Leu Lys Tyr Ile Val Met Phe Leu Glu Asn Lys His Phe Gly Thr Val 290 295 300
- Glu Gly Ser Ser Arg Leu His Pro Gly Lys Asn Lys Cys Pro Phe Ser 305 310 315 320
- Asp Arg Ser Ser Ser Leu Glu Ala Met Ala Ser Lys Leu Met Glu Ile. 325 330 335
- Leu Gln Glu Phe Thr Glu Ser Asn Thr Leu His Lys Ser Leu Thr Gly 340 345 350
- Ser Leu Gly Ser Ser His Leu Glu Lys Thr Glu Phe Arg Pro Ala His 355 360 365
- Lys Asp Phe Gln Cys Val Leu Thr Arg Asp Gln Ser Ile Asn Leu Cys 370 375 380
- Asp Ile Leu Ser Leu Val Glu Leu Ile Ala Cys Tyr Thr Ala Trp Asp. 385 390 395 400
- Trp Thr Ser Ala Asn Ile Val Ala Pro Leu Leu Lys Met Leu Gly Met 405 410 415
- Pro Leu Pro Met Asn Leu Ser Val Ala Ile Val Ser Leu Leu Gly Gln 420 425 430
- Leu Ser Ser Ile Gly Val Asp Ala Gly Gly Tyr Glu Asn Glu Gly Ile 435 440 445
- Ser Asn Leu Arg Val Lys Leu Ser Ala Phe Leu Gln Cys Glu Thr Thr 450 455 460
- Leu Lys Ala Gly Phe Ala Val Gln Ile Ala Thr Val Ser Ser Leu Leu 465 470 475 480
- Lys Thr Leu Gln Leu Lys Phe Pro Ile Asp Phe Gln Asp Lys Thr Thr 485 490 495
- Met Ile Pro Gly Ser Gly Asp Gln Ser Leu Ser Gly Ser Val Asn Val 500 505 510

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Val Thr Lys Trp Leu Ser Leu Leu Ser Lys Glu Gln Arg Val Phe Ala 515

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<210> 47

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<223> 31895

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Pro Phe Pro Val Pro Ile Val Asp Leu Arg Arg Ala Ala Arg Glu Arg

gtc aag aac aac aaa gac aaa cct aag aga cct cta cct ccg cct aaa

384

Val	Lys	Asn 115		a Ly	s A	sp L		ro 1	Lys i	Arg	Pro	Leu	Pro	o P 5	ro :	Pro	Lу	/S	
aat Asn	ggt Gly 130	atg Met	gti Va	t gt 1 Va	ga al L	ys S	gc c er I .35	ett Geu	gtg Val	cct Pro	ctt Leu	gct Ala 140	. 1y	t a r I	aa ys	gta Val	ta Ty	ac Yr	432
aat Asn 145	gca Ala	aga Arg	at JIl	c ag e Ai	rg L	tg a eu I 50	itc a [le ]	aac Asn	aat Asn	ctc Leu	cac His 155	cgg	g ct g L∈	t a eu N	atg 1et	aaa Lys	V	tt al 60	480
gtt Val	cgt Arg	gtt Va:	aa L As	n A	ct t la C 65	gt g ys (	sly '	tgg Trp	tgc Cys	aat Asn 170	gag Glu	att Ile	e Hi	at g is \	gtt Val	gga Gly 175	-	ct ro	528
tat Tyr	Gly 999	cat Hi	t cc s Pr 18	O P	tt a he I	ag t Jys s	cg Ser	tgt Cys	aaa Lys 185	ggt Gly	Pro	aat As:	t ac	ur.	tcc Ser 190	caa Glr	a n A	rg gg	576
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cct Pro	ctto Let	ı Gl	ago uA:	cc t la T	at d	His	ctt Leu 215	ttt Phe	gac Asp	ege Arg	ctt	gg 1 Gl 22	λг	ag ys	cgt Arg	ato Ile	e A	egt Arg	672
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tg:	c at	t ca e Gl	g g n G	ly (	ggc Gly 245	gtt Val	gaa Glu	ata Ile	ccc Pro	gaa Glu 250	ı Pn	t co e Pi	a g	gca Ala	aaa Lys	ag Ar 25	9	aga Arg	768
ag Ar	a aa g Ly	a co s Pi	o I	tt a le :	atc Ile	cgc Arg	att Ile	Gly	265	a ago s Sei	ga Gl	g ti u Pl	tt g ne V	gtt Val	gat Asp 270	בא כ	a .a	gat Asp	816
ga Gl	a ac u Th	r G	aa t Lu L 75	tg ( ieu 1	cct Pro	gat Asp	cca Pro	gaç Glu 280	ı Pro	cag o Gl	g cc n Pr	t co to P	FO .	cca Pro 285	va.	g co l Pr	ea co	ttg Leu	864
tt Le	a ac u Th	r G	ag t lu I	ta Leu	cct Pro	gtc Val	tca Ser 295	GI	g ate	c ac e Th	t co r Pi	.0 P	ca ro 00	tct Ser	ag Se	c ga r G	aa lu	gaa Glu	912
ga G1 - 30	u Tì	ea g nr V	tc t al S	cc Ser	tta Leu	gcc Ala 310	Glu	ga:	a ac u Th	a tt r Le	u G.	ag g ln A 15	cc la	tgg	g ga o Gl	a ga u G	aa lu	atg Met 320	960
ag Ai	ga go	ca g la G	ga q ly 1	gcc Ala	aaa Lys 325	aag Lys	cto Lev	g at 1 Me	g ag t Ar	g at g Me 33	t T	ac a yr P	rg ugg	gtt Val	ag l Ar	y v	tc al 35	tgt Cys	1008
G:	gg t ly T	ac t yr C	ys :	cca Pro 340	gag Glu	gtt Val	cac His	gt Va	a gg 1 Gl 34	y Pi	ca a	cg c	gga Bly	Cac	c as s Ly 35	SP	cc la	cag Gln	1056
a	ac t	gt g	gt (	gca	ttc	aaç	g ca	c ca	a ca		gg a	at 9	ggc	ca	g ca	at g	gt	tgg	1104

Asn Cys Gly Ala Phe Lys His Gln Gln Arg Asn Gly Gln His Gly Trp 355 caa tot goa gta ott gac gac ttg ata cog coa aga tat gtt tgg cat 1152 Gln Ser Ala Val Leu Asp Asp Leu Ile Pro Pro Arg Tyr Val Trp His 380 gtt cct gat gtg aat ggg cca deg atg cag cga gag cta cga agc ttc 1200 Val Pro Asp Val Asn Gly Pro Pro Met Gln Arg Glu Leu Arg Ser Phe 390 tac ggg caa gca cct gct gtt gtg gag ata tgt gct cag gct ggc gct 1248 Tyr Gly Gln Ala Pro Ala Val Val Glu Ile Cys Ala Gln Ala Gly Ala gtt gta cct gag cat tat aga gct aca atg aga ctg gag gtt gga att 1296 Val Val Pro Glu His Tyr Arg Ala Thr Met Arg Leu Glu Val Gly Ile 425 1332 cct tcg agt gtg aaa gaa gct gag atg gtt gtt tga Pro Ser Ser Val Lys Glu Ala Glu Met Val Val 440

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<213> Arabidopsis thaliana

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Ser Pro Lys Ser Val Pro Phe Ala Ile His Ser Val Thr Arg Arg Gln 20 25 30

Phe Leu Asn Pro Asn Thr Phe Tyr Arg Phe Gly Phe Ser Pro Ser Leu 35 40 45

Gln Gly Ser Ser Ile Glu Phe Ser Leu Gln Leu Asn Ser Arg Val Val 50 55 60

Leu Ser Lys Glu Arg Arg Ser Leu Pro Leu Val Val Arg Asn Asp Arg 65 70 75 80

Pro Gln Asn Glu Asp Leu Pro Lys Gln Tyr Thr Arg Arg Glu Lys Lys 85 90 95

Pro Phe Pro Val Pro Ile Val Asp Leu Arg Arg Ala Ala Arg Glu Arg 100 105 110

- Val Lys Asn Asn Lys Asp Lys Pro Lys Arg Pro Leu Pro Pro Pro Lys 115 120 125
- Asn Gly Met Val Val Lys Ser Leu Val Pro Leu Ala Tyr Lys Val Tyr 130 135 140
- Asn Ala Arg Ile Arg Leu Ile Asn Asn Leu His Arg Leu Met Lys Val 145 150 155 160
- Val Arg Val Asn Ala Cys Gly Trp Cys Asn Glu Ile His Val Gly Pro 165 170 175
- Tyr Gly His Pro Phe Lys Ser Cys Lys Gly Pro Asn Thr Ser Gln Arg 180 185 190
- Lys Gly Leu His Glu Trp Thr Asn Ser Val Ile Glu Asp Val Ile Val 195 200 205
- Pro Leu Glu Ala Tyr His Leu Phe Asp Arg Leu Gly Lys Arg Ile Arg 210 215 220
- His Asp Glu Arg Phe Ser Ile Pro Arg Val Pro Ala Val Val Glu Leu 225 230 235 240
- Cys Ile Gln Gly Gly Val Glu Ile Pro Glu Phe Pro Ala Lys Arg Arg 255
- Arg Lys Pro Ile Ile Arg Ile Gly Lys Ser Glu Phe Val Asp Ala Asp 260 265 270
- Glu Thr Glu Leu Pro Asp Pro Glu Pro Gln Pro Pro Pro Val Pro Leu 275 280 285
- Leu Thr Glu Leu Pro Val Ser Glu Ile Thr Pro Pro Ser Ser Glu Glu 290 295 300
- Glu Thr Val Ser Leu Ala Glu Glu Thr Leu Gln Ala Trp Glu Glu Met 305 310 315 320
- Arg Ala Gly Ala Lys Lys Leu Met Arg Met Tyr Arg Val Arg Val Cys 325 330 335

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Gly Tyr Cys Pro Glu Val His Val Gly Pro Thr Gly His Lys Ala Gln 350 345 Asn Cys Gly Ala Phe Lys His Gln Gln Arg Asn Gly Gln His Gly Trp 360 355 Gln Ser Ala Val Leu Asp Asp Leu Ile Pro Pro Arg Tyr Val Trp His 375 Val Pro Asp Val Asn Gly Pro Pro Met Gln Arg Glu Leu Arg Ser Phe 390 Tyr Gly Gln Ala Pro Ala Val Val Glu Ile Cys Ala Gln Ala Gly Ala 410 Val Val Pro Glu His Tyr Arg Ala Thr Met Arg Leu Glu Val Gly Ile Pro Ser Ser Val Lys Glu Ala Glu Met Val Val <210> 49 <211> 540 <212> DNA <213> Arabidopsis thaliana <220> <221> CDS <222> (1)..(540) <223> 34269 <400> 49 atg tta tca agc att gtt gtt gtc acc agg atc gaa aat ttt caa 48 Met Leu Ser Ser Ile Val Val Val Thr Arg Ile Glu Asn Phe Gln tgt tgt tgt ttg aga gag atg atg gct gcg aag ctt cag aaa tgg cga 96 Cys Cys Leu Arg Glu Met Met Ala Ala Lys Leu Gln Lys Trp Arg aat ctg gca ggt cgt cta gat ctg atg aat cgg agc ggc gct gtg tcg 144 Asn Leu Ala Gly Arg Leu Asp Leu Met Asn Arg Ser Gly Ala Val Ser

40

45

35

acg Thr	agg Arg 50	cgg Arg	ttc Phe	ctg Leu	cac His	gaa Glu 55	ggt Gly	cca Pro	gat Asp	Thr	gtg Val 60	gag Glu	gag Glu	ctt Leu	ctc Leu	192
gaa Glu 65	aga Arg	cat His	cta Leu	gcg Ala	aag Lys 70	aaa Lys	gag Glu	aaa Lys	cca Pro	ata Ile 75	atc Ile	gat Asp	cac His	gat Asp	gag Glu 80	240
gct Ala	gag Glu	ttt Phe	ctg Leu	aat Asn 85	aga Arg	cgg Arg	cgt Arg	ctg Leu	acg Thr 90	agc Ser	acg Thr	cgc Arg	cgg Arg	gaa Glu 95	gcg Ala	288
ttg Leu	agt Ser	ttg Leu	tac Tyr 100	aga Arg	gac Asp	ata Ile	tta Leu	cga Arg 105	gcg Ala	act Thr	cgg Arg	ttc Phe	ttc Phe .110	acg Thr	tgg Trp	336
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agg Arg	aag Lys 130	Glu	ttt Phe	gaa Glu	gcg Ala	gcg Ala 135	cga Arg	ttt	gag Glu	acg Thr	gat Asp 140	ccg Pro	gag Glu	gtt Val	atc Ile	 432
aca Thr 145	Arg	ctt Leu	ctg Leu	ata Ile	ggt Gly 150	Gly	agc Ser	gac Asp	gcc Ala	gtt Val 155	Ser	tct Ser	gct Ala	tta Leu	gat Asp 160	480
aag Lys	ctt Leu	gcg Ala	gag Glu	aag Lys 165	Gln	aga Arg	gag Glu	atg Met	att Ile	Glu	aaa Lys	a caa s Glr	cgo Arg	cgt J Arg 175	ggt Gly	528
		cgc Arg		L											•	540

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Asn Leu Ala Gly Arg Leu Asp Leu Met Asn Arg Ser Gly Ala Val Ser 35 40 45

Thr Arg Arg Phe Leu His Glu Gly Pro Asp Thr Val Glu Glu Leu Leu 50 55 60

Glu Arg His Leu Ala Lys Lys Glu Lys Pro Ile Ile Asp His Asp Glu 65 70 - 75 80

Ala Glu Phe Leu Asn Arg Arg Arg Leu Thr Ser Thr Arg Arg Glu Ala 85 90 95

Leu Ser Leu Tyr Arg Asp Ile Leu Arg Ala Thr Arg Phe Phe Thr Trp

Ile Asp Ser Arg Gly Asn Leu Trp Arg Asp Val Leu Arg Glu Asn Ala 115 120 125

Arg Lys Glu Phe Glu Ala Ala Arg Phe Glu Thr Asp Pro Glu Val Ile 130 135 140

Thr Arg Leu Leu Ile Gly Gly Ser Asp Ala Val Ser Ser Ala Leu Asp 145 150 155 160

Lys Leu Ala Glu Lys Gln Arg Glu Met Ile Glu Lys Gln Arg Gly 165 170 175

Asp Gln Arg

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<223> 34540

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gct Ala	cat His	cag Gln 35	att Ile	cca Pro	gat Asp	acc Thr	ctc Leu 40	ctc Leu	tcg Ser	ctt Leu	cag Gln	cat His	cca Pro	cc: Pr	a a o T	ct hr	144
tat Tyr	acg Thr 50	ctc Leu	gga Gly	aag Lys	cgt Arg	aga Arg 55	acc Thr	gat Asp	cac His	aat Asn	cta Lev 60	cti Lei	ato 1 Ile	c cc	t g	jaa Hu	192
tct Ser 65	gaa Glu	ctt Leu	aca Thr	aaa Lys	atc Ile 70	gga Gly	gct Ala	gaa Glu	ctt Leu	cat His 75	tat Tyi	ac'	t caa r Gli	a ag	9 '	gga Bly B0	240
gga Gly	gac Asp	atc Ile	acc Thr	ttc Phe 85	cat His	ggc Gly	cct Pro	cat His	caa Gln 90	gco Ala	ate	c tt e Le	a tai u Ty:	t co r Pr 95	.0 .	atc Ile	288
att Ile	tcc Ser	tta Leu	cgc Arg 100	Ser	att Ile	ggt Gly	ttt Phe	ggt Gly 105	Ala	agg Arg	g aa g As	c ta n Ty	c gt r Va 11	T G.	ag Lu	aca Thr	336
ttg Leu	gag Glu	cgg Arg	, Ser	atg Met	atc : Ile	gag Glu	ttt Phe 120	: Ala	t tog a Sei	g at	t ta e Ty	t gg r G] 12	gc gt .y Va !5	g a	aa ys	gct Ala	384
cga Arg	gca J Ala 130	Gly	a aac / Asr	aaa Lys	tgt Cys	gag Glu 135	Thr	999 Gly	g gti y Vai	t tg 1 Tr	g gt p Va 14	II G.	gg ga ly As	it a sp A	gg rg	aag Lys	432
ato Ile 145	e Gl	gct Ala	atta Ile	= Gly	g gtt 7 Val 150	Arg	g ata	a to e Se	t tc r Se	t gg r Gl 15	A T	c a	ct ag hr Se	gt c er H	at is	ggt Gly 160	480
tt: Le:	g gc	c tt a Le	a aat u Ası	t ata n Ile 16	e Ası	cct Pro	gai Asj	t at p Me	g aa t Ly 17	s 13	c ti r Pl	t g ne G	ag ca lu H	rs 1	tt le .75	gtg Val	528
cc Pr	t tg o Cy	t gg s Gl	g at y Il 18	e Al	t gai a Asj	t aaa p Lys	a ga s Gl	a gt u Va 18	I Th	a to r Se	et t	tg c eu A	ga a rg A 1	ga g rg ( 90	gag Slu	acg Thr	576
ga As	t ac p Th	t ct r Le 19	u Le	t cc u Pr	t tc o Se	a ga r Gl	a ga u Gl 20	u Va	g at	t ca le H	at g is G	Iu c	ag t ln L	tg g	gtt Val	tct Ser	624
tg Cy	t tt s Le 21	u Al	c aa .a Ly	a go s Al	g tt a Ph	t tc e Se 21	r Ty	it ga r As	at ga sp As	at g sp V	al v	tc tal 7	gg a	ys iag	gaa Glu	gat Asp	672
cc Pr 22	o Se	a ct er Le	c at u Il	t tt .e Le	g ga eu As 23	p Th	c ca r Gl	aa ga ln Aa	at a sp L	ys G	aa t lu 35	aa					708

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<211> 235

<212> PRT

<213> Arabidopsis thaliana

<400> 52

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Tyr Leu Lys Ser Leu Lys Leu Gln Glu Lys Leu Val Ser Glu Arg Lys 20 25 30

Ala His Gln Ile Pro Asp Thr Leu Leu Ser Leu Gln His Pro Pro Thr 35 40 45

Tyr Thr Leu Gly Lys Arg Arg Thr Asp His Asn Leu Leu Ile Pro Glu 50 55 60

Ser Glu Leu Thr Lys Ile Gly Ala Glu Leu His Tyr Thr Gln Arg Gly 65 70 75 80

Gly Asp Ile Thr Phe His Gly Pro His Gln Ala Ile Leu Tyr Pro Ile 85 90 95

Ile Ser Leu Arg Ser Ile Gly Phe Gly Ala Arg Asn Tyr Val Glu Thr 100 105 110

Leu Glu Arg Ser Met Ile Glu Phe Ala Ser Ile Tyr Gly Val Lys Ala 115 120 125

Arg Ala Gly Asn Lys Cys Glu Thr Gly Val Trp Val Gly Asp Arg Lys 130 135 140

Ile Gly Ala Ile Gly Val Arg Ile Ser Ser Gly Ile Thr Ser His Gly
145 150 155 160

Leu Ala Leu Asn Ile Asp Pro Asp Met Lys Tyr Phe Glu His Ile Val 165 170 175

Pro Cys Gly Ile Ala Asp Lys Glu Val Thr Ser Leu Arg Arg Glu Thr 180 185 190

Asp Thr Leu Leu Pro Ser Glu Glu Val Ile His Glu Gln Leu Val Ser 195 200 205

Cys Leu Ala Lys Ala Phe Ser Tyr Asp Asp Val Val Trp Lys Glu Asp 210 215 220

Pro Ser Leu Ile Leu Asp Thr Gln Asp Lys Glu 225 230 235

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105

110

acg agt gat gat gat aat gat tot to aaag act ggt gtt gaa ttg ott Thr Ser Asp Asp Asp Asp Ser Ser Lys Thr Gly Val Glu Leu Leu 115 120 125	384
tgt gtg gtg aga gct gtg ttg aag aaa ata cga agg aga gtt tta gtt Cys Val Val Arg Ala Val Leu Lys Lys Ile Arg Arg Arg Val Leu Val 130 135 140	432
gga gat aag gtt ctt gtt gga tct att gat tgg gtt gat aga aga gga Gly Asp Lys Val Leu Val Gly Ser Ile Asp Trp Val Asp Arg Arg Gly 145 150 155 160	480
atg att gag aat gtg ttt cat cga cgt tcg gag att ttg gat cca cct Met Ile Glu Asn Val Phe His Arg Arg Ser Glu Ile Leu Asp Pro Pro 165 170 175	528
gtt gcg aac gtt gat cat ttg ctt gtt ctt ttc tct ttg gat caa ccg Val Ala Asn Val Asp His Leu Leu Val Leu Phe Ser Leu Asp Gln Pro 180 185 190	576
aaa ctt gag ccg ttt act ctt act agg ttc ttg gtg gaa gct gaa tct Lys Leu Glu Pro Phe Thr Leu Thr Arg Phe Leu Val Glu Ala Glu Ser 195 200 205	624
act cgt att cca tta aca ctt gct ttg aat aaa act gaa ctc att agt Thr Arg Ile Pro Leu Thr Leu Ala Leu Asn Lys Thr Glu Leu Ile Ser 210 215 220	672
gaa gag gaa ttg gaa act tgg aag ata agg ttg cgt gga tgg aac tat Glu Glu Glu Leu Glu Thr Trp Lys Ile Arg Leu Arg Gly Trp Asn Tyr 225 230 235 240	720
gaa cca ttg ttt tgt agt gtg gga act aaa gat gga ctt gat gat att Glu Pro Leu Phe Cys Ser Val Gly Thr Lys Asp Gly Leu Asp Asp Ile 245 250 255	768
gcg ttt gtt ctg aga gat cag act tct gtg att gtt gga cct agt ggt Ala Phe Val Leu Arg Asp Gln Thr Ser Val Ile Val Gly Pro Ser Gly 260 265 270	816
gtt gga aag tcg agt tta atc aac gta ttg agg agt aat cat ggt ggt Val Gly Lys Ser Ser Leu Ile Asn Val Leu Arg Ser Asn His Gly Gly 275 280 285	864
ggt gtg gtg gaa gat gag aat tgg ttt gag cct atg tta ggt aat aag Gly Val Val Glu Asp Glu Asn Trp Phe Glu Pro Met Leu Gly Asn Lys 290 295 300	912
tgg ttt gat gat cag cga gta ggg gaa gtt tcg agt aga agt ggt aga Trp Phe Asp Asp Gln Arg Val Gly Glu Val Ser Ser Arg Ser Gly Arg 305 310 315	960
ggt aaa cat aca aca cga aat gta tcg cta ctg ccg gtt tct gaa ggt Gly Lys His Thr Thr Arg Asn Val Ser Leu Leu Pro Val Ser Glu Gly 335	1008
ggt tac ctc gct gat act cct ggc ttt aac cag cct agt ttg ctg aaa Gly Tyr Leu Ala Asp Thr Pro Gly Phe Asn Gln Pro Ser Leu Leu Lys 340 345	1056

Ş	gta /al	acg Thr	aag Lys 355	cat His	tca Ser	cta Leu	Ala	cac His 360	tgt Cys	ttt Phe	cct Pro	gag Glu	ata Ile 365	cgg Arg	aac Asn	atg Met	1104
	att Ile	gag Glu 370	agc Ser	gaa Glu	aaa Lys	tgt Cys	gga Gly 375	ttc Phe	aga Arg	gac Asp	tgc Cys	ttg Leu 380	cat His	att Ile	Gly 999	gaa Glu	1152
	cca Pro 385	gga Gly	tgt Cys	gtt Val	gtg Val	aaa Lys 390	ggt Gly	gac Asp	tgg Trp	gaa Glu	agg Arg 395	tat Tyr	cct Pro	tac Tyr	tac Tyr	tta Leu 400	1200
	caa Gln	ttg Leu	ctt Leu	gat Asp	gag Glu 405	atc Ile	aga Arg	atc Ile	agg Arg	gaa Glu 410	gaa Glu	ttt Phe	cag Gln	ctt Leu	agg Arg 415	act Thr	1248
	ttt Phe	gga Gly	acc Thr	aaa Lys 420	agg Arg	gaa Glu	gat Asp	gat Asp	gtt Val 425	agg Arg	tac Tyr	aag Lys	gtg Val	gga Gly 430	gac Asp	atg Met	1296
	ggt Gly	gtg Val	aaa Lys 435	cat His	gct Ala	gaa Glu	cca Pro	cgg Arg 440	Leu	atg Met	cct Pro	aag Lys	aag Lys 445	His	agg Arg	aga Arg	1344
	gag Glu	tca Ser 450	Arg	aag Lys	aaa Lys	acg Thr	aaa Lys 455	Gln	aca Thr	atg Met	ato Ile	agt Ser 460	GIU	ctg Leu	gat Asp	gag Glu	1392
	ttc Phe 465	Glu	gat Asp	gaa Glu	gac Asp	agt Ser 470	Asp	ttg Leu	tac Tyr	ata : Ile	gag Glu 475	ı Asr	gac Asp	cca Pro	ato Ile	gtc Val 480	1440
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<211> 490

<212> PRT

<213> Arabidopsis thaliana

<400> 54

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Arg His Thr Ala Ile Phe His Gly Gly Val Gly Val Arg Phe Lys Phe 20 25 30

Leu Arg Ser Phe Ser Pro Leu Ser Ala Arg Arg Asp Asn Pro Asp Val 35 40 45

Ser Arg Lys Pro Gln Pro Ser Lys Asn Met Leu Arg Ala Lys His Ile 50 60

Gly Lys Asn Tyr Ser Ser Ser Leu Ser Pro Val Leu Ser Pro Glu His 65 70 75 80

Lys Pro Ser Leu Leu Glu Ser Gln Ala Ile Gly Thr Val Ala Thr Ala 85 90 95

Gln Ala Asn Phe Met Arg Val Ile Val Gln Asp Val Ala Asn Ser Val 100 105 110

Thr Ser Asp Asp Asp Asn Asp Ser Ser Lys Thr Gly Val Glu Leu Leu 115 120 125

Cys Val Val Arg Ala Val Leu Lys Lys Ile Arg Arg Arg Val Leu Val

Gly Asp Lys Val Leu Val Gly Ser Ile Asp Trp Val Asp Arg Arg Gly 145 150 155 160

Met Ile Glu Asn Val Phe His Arg Arg Ser Glu Ile Leu Asp Pro Pro 165 170 175

Val Ala Asn Val Asp His Leu Leu Val Leu Phe Ser Leu Asp Gln Pro 180 185 190

Lys Leu Glu Pro Phe Thr Leu Thr Arg Phe Leu Val Glu Ala Glu Ser 195 200 205

Thr Arg Ile Pro Leu Thr Leu Ala Leu Asn Lys Thr Glu Leu Ile Ser 210 215 220

Glu Glu Glu Leu Glu Thr Trp Lys Ile Arg Leu Arg Gly Trp Asn Tyr 225 230 235 240

Glu Pro Leu Phe Cys Ser Val Gly Thr Lys Asp Gly Leu Asp Asp Ile 245 250 255

Ala Phe Val Leu Arg Asp Gln Thr Ser Val Ile Val Gly Pro Ser Gly 260 265 270

Val Gly Lys Ser Ser Leu Ile Asn Val Leu Arg Ser Asn His Gly Gly 275 280 285

Gly Val Val Glu Asp Glu Asn Trp Phe Glu Pro Met Leu Gly Asn Lys 290 295 300

Trp Phe Asp Asp Gln Arg Val Gly Glu Val Ser Ser Arg Ser Gly Arg 305 310 315 320

Gly Lys His Thr Thr Arg Asn Val Ser Leu Leu Pro Val Ser Glu Gly 325 330 335

Gly Tyr Leu Ala Asp Thr Pro Gly Phe Asn Gln Pro Ser Leu Leu Lys 340 345 350

Val Thr Lys His Ser Leu Ala His Cys Phe Pro Glu Ile Arg Asn Met 355 360 365

Ile Glu Ser Glu Lys Cys Gly Phe Arg Asp Cys Leu His Ile Gly Glu 370 375 380

Pro Gly Cys Val Val Lys Gly Asp Trp Glu Arg Tyr Pro Tyr Tyr Leu 385 390 395 400

Gln Leu Leu Asp Glu Ile Arg Ile Arg Glu Glu Phe Gln Leu Arg Thr 405 410 415

Phe Gly Thr Lys Arg Glu Asp Asp Val Arg Tyr Lys Val Gly Asp Met 420 425 430

Gly Val Lys His Ala Glu Pro Arg Leu Met Pro Lys Lys His Arg Arg 435 440 445

Glu Ser Arg Lys Lys Thr Lys Gln Thr Met Ile Ser Glu Leu Asp Glu 450 455 460

Phe Glu Asp Glu Asp Ser Asp Leu Tyr Ile Glu Asn Asp Pro Ile Val 465 470 475 480

Gln Ala Ile Glu Asn Glu Asn Lys Arg Gln 485 490

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<211> 897

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<213> Arabidopsis thaliana

<220>

<221> CDS

<222> (1)..(897)

<223> 35154

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act Thr	tat Tyr	tgc Cys	aat Asn 20	gga Gly	atg Met	tct Ser	cag Gln	ttc Phe 25	ctc Leu	tct Ser	cta Leu	atg Met	ggc Gly 30	agg Arg	aag Lys	96	
gtt Val	gct Ala	att Ile 35	gtt Val	aat Asn	ctg Leu	gat Asp	cct Pro 40	gca Ala	aat Asn	gat Asp	gca Ala	tta Leu 45	cct Pro	tat Tyr	gag Glu	144	
tgt Cys	ggt Gly 50	gtg Val	aat Asn	ata Ile	gaa Glu	gaa Glu 55	ttg Leu	atc Ile	aag Lys	tta Leu	gaa Glu 60	gat Asp	gtt Val	atg Met	tcg Ser	192	
gaa Glu 65	cac His	tcg Ser	ctt Leu	ggt Gly	cct Pro 70	aat Asn	gga Gly	ggt Gly	ctt Leu	gta Val 75	tat Tyr	tgt Cys	atg Met	gag	tac Tyr 80	240	
ttg Leu	gag Glu	aaa Lys	aac Asn	att Ile 85	gac Asp	tgg Trp	ctg Leu	gaa Glu	tct Ser 90	aaa Lys	cta Lev	aag Lys	cct Pro	ctt Lev 95	ctg Leu	288	
aag Lys	gat Asp	cat His	tac Tyr 100	Ile	ctc Leu	ttt Phe	gat Asp	ttt Phe 105	Pro	ggc Gly	caa Glr	a gtg n Val	g gaa L Glu 110	r ne	ttc Phe	336	
tto Phe	att Ile	cat His	Asp	agt Ser	acc Thr	aag Lys	aat Asr 120	ı Va.	cto Lev	acg Thi	g aaq c Ly	g cto s Let 12	7 77	t aa: e Ly	a tca s Ser	384	
tto Lev	g aac 1 Asr 130	ı Leı	aga Arg	tta J Lev	a act 1 Thr	gct Ala 135	Va.	g caa L Gli	a cta n Lev	a ati	t ga e As 14	р ъе	c ca r Hi	t ct s Le	a tgt u Cys	432	
tgt Cys 14!	s Ası	cco Pro	c ggg	g aac ⁄ Ası	tac 1 Tyr 150	· Val	a agt	t to r Se	g cta r Le	a ct u Le 15	u ne	c tc u Se	c tt r Le	a to u Se	c aca r Thr 160	480	
at: Me	g cti t Lei	t cae u Hi	c ato	g gaa t Gli 16	u Lei	c cca	a ca o Hi	t gt s Va	c aa l As 17	n va	a tt l Le	g to eu Se	t aa er Ly	S 11	c gat e Asp 5	528	

ctg Leu	att Ile	gga Gly	agc Ser 180	tac Tyr	Gly 999	aag Lys	cta Leu	gct Ala 185	ttc Phe	aat Asn	tta Leu	gat Asp	ttc Phe 190	tat Tyr	acc Thr		576
gat Asp	gtt Val	caa Gln 195	gac Asp	ttg Leu	tca Ser	tac Tyr	ttg Leu 200	gag Glu	cac His	cat His	ctt Leu	agt Ser 205	caa Gln	gat Asp	cct Pro		624
cgc Arg	tct Ser 210	gct Ala	aag Lys	tac Tyr	aga Arg	aaa Lys 215	cta Leu	aca Thr	aaa Lys	gag Glu	cta Leu 220	tgt Cys	agt Ser	gtc Val	att Ile		672
gaa Glu 225	gat Asp	tac Tyr	agt Ser	ctt Leu	gtt Val 230	aat Asn	ttt Phe	aca Thr	acc Thr	ttg Leu 235	gat Asp	att Ile	cag Gln	gat Asp	aaa Lys 240		720
gaa Glu	agt Ser	gtt Val	gly aaa	gat Asp 245	Leu	gta Val	aag Lys	ctc Leu	atc Ile 250	Asp	aag Lys	agc Ser	aat Asn	gga Gly 255	tac Tyr		768
ata Ile	ttt Phe	gcc Ala	ggc Gly 260	Ile	gat Asp	gca Ala	agt Ser	gtg Val 265	Val	gaa Glu	tac Tyr	ago Ser	aag Lys 270	TTE	gca Ala		816
att Ile	ggt Gly	caa Glr 275	Thr	gat Asp	tgg Trp	gat Asp	tat Tyr 280	Asr	aga Arg	gto y Val	gca L Ala	a gct a Ala 28!	ı va.	a cag L Gli	g gag n Glu	·	864
aag Lys	tac Tyr 290	Met	g gaa : Glu	ı gat ı As <u>r</u>	gag Glu	gaa Glu 295	ı Ile	a caa e Glr	a gad n Asp	tga P	<b>a</b>				·		897

<210> 56

<211> 298

<212> PRT

<213> Arabidopsis thaliana

<400> 56

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Thr Tyr Cys Asn Gly Met Ser Gln Phe Leu Ser Leu Met Gly Arg Lys 20 25 30

Val Ala Ile Val Asn Leu Asp Pro Ala Asn Asp Ala Leu Pro Tyr Glu 35 40 45

Cys Gly Val Asn Ile Glu Glu Leu Ile Lys Leu Glu Asp Val Met Ser 50 55 60

Glu His Ser Leu Gly Pro Asn Gly Gly Leu Val Tyr Cys Met Glu Tyr 65 70 75 80

Leu Glu Lys Asn Ile Asp Trp Leu Glu Ser Lys Leu Lys Pro Leu Leu 85 90 95

Lys Asp His Tyr Ile Leu Phe Asp Phe Pro Gly Gln Val Glu Leu Phe 100 105 110

Phe Ile His Asp Ser Thr Lys Asn Val Leu Thr Lys Leu Ile Lys Ser 115 120 125

Leu Asn Leu Arg Leu Thr Ala Val Gln Leu Ile Asp Ser His Leu Cys 130 135 140

Cys Asp Pro Gly Asn Tyr Val Ser Ser Leu Leu Ser Leu Ser Thr 145 150 155 160

Met Leu His Met Glu Leu Pro His Val Asn Val Leu Ser Lys Ile Asp 165 170 175

Leu Ile Gly Ser Tyr Gly Lys Leu Ala Phe Asn Leu Asp Phe Tyr Thr 180 185 190

Asp Val Gln Asp Leu Ser Tyr Leu Glu His His Leu Ser Gln Asp Pro 195 200 205

Arg Ser Ala Lys Tyr Arg Lys Leu Thr Lys Glu Leu Cys Ser Val Ile 210 215 220

Glu Asp Tyr Ser Leu Val Asn Phe Thr Thr Leu Asp Ile Gln Asp Lys 225 230 235 240

Glu Ser Val Gly Asp Leu Val Lys Leu Ile Asp Lys Ser Asn Gly Tyr 245 250 255

Ile Phe Ala Gly Ile Asp Ala Ser Val Val Glu Tyr Ser Lys Ile Ala 260 265 270

Ile Gly Gln Thr Asp Trp Asp Tyr Asn Arg Val Ala Ala Val Gln Glu 275 280 285

Lys Tyr Met Glu Asp Glu Glu Ile Gln Asp 290 295

<210> 57

<211> 849

<212> DNA

<213> Arabidopsis thaliana

<220>

<221> CDS

<222> (1)..(849)

<223> 35438

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aag Lys	aag Lys	aaa Lys	tat Tyr 20	tcc Ser	gaa Glu	tac Tyr	gat Asp	gag Glu 25	att Ile	aat Asn	aag Lys	gaa Glu	caa Gln 30	gaa Glu	gag Glu		96
aaa Lys	ttc Phe	ctt Leu 35	acc Thr	ttt Phe	gtt Val	tca Ser	gcc Ala 40	tca Ser	gag Glu	gag Glu	ttg Leu	atg Met 45	gaa Glu	cat His	ttg Leu		144
aga Arg	ggt Gly 50	gaa Glu	aat Asn	cag Gln	agt Ser	tct Ser 55	ctg Leu	gag Glu	atg Met	gtt Val	gag Glu 60	aag Lys	ttg Leu	agg Arg	aat Asn		192
gaa Glu 65	atc Ile	att Ile	tca Ser	atc Ile	aga Arg 70	tct Ser	ggc Gly	agg Arg	gac Asp	gac Asp 75	aag Lys	ttt Phe	ctg Leu	gag Glu	tgt Cys 80		240
caa Gln	aag Lys	ctt Leu	ctc Leu	atg Met 85	gaa Glu	gaa Glu	gaa Glu	cta Leu	aag Lys 90	aac Asn	aaa Lys	tca Ser	ctt Leu	tct Ser 95	gaa Glu		288
gaa Glu	gtt Val	gtc Val	aag Lys 100	Leu	aaa Lys	gag Glu	ctg Leu	gtc Val 105	Gln	gag Glu	gaa Glu	cat His	cct Pro	Arg	aac Asn		336
tat Tyr	gaa Glu	gat Asp 115	Gln	agt Ser	gga Gly	aaa Lys	aaa Lys 120	Glr	aag Lys	aga Arg	aag J <b>L</b> ys	act Thr 125	Pro	gaa Glu	agt Ser		384
gct Ala	cga Arg	Val	aca Thr	acg Thr	aga Arg	agc Ser 135	Met	ata Ile	aaa Lys	cgt Arg	ago Ser 140	: Arg	t ctg J Lei	g tca 1 Sei	gaa Glu	٠	432
gat	ttg	gtg	gaa	acg	gat	atg	gta	tca	a cct	gad	att	age	c aaa	a cat	cat		480

Asp 145	Leu	Val	Glu	Thr	Asp 150	Met	Val	Ser	Pro	Asp 155	Ile	Ser	Lys	His	His 160	
aaa Lys	gca Ala	aag Lys	gag Glu	cct Pro 165	ctc Leu	ttg Leu	gtt Val	tct Ser	cag Gln 170	cca Pro	caa Gln	tgc Cys	tgc Cys	aga Arg 175	aca Thr	528
acc Thr	tac Tyr	gat Asp	gga Gly 180	tca Ser	agt Ser	agt Ser	tct Ser	gct Ala 185	agt Ser	tgt Cys	aca Thr	ttt Phe	caa Gln 190	gct Ala	ctt Leu	576
ggc Gly	aaa Lys	cac His 195	ttg Leu	cta Leu	gga Gly	atg Met	aaa Lys 200	tta Leu	tca Ser	act Thr	aat Asn	aat Asn 205	aag Lys	ggc	aaa Lys	624
cgc Arg	gcc Ala 210	Cys	att Ile	gta Val	gcc Ala	tca Ser 215	cac His	cca Pro	aca Thr	acc Thr	ggt Gly 220	Leu	tcc Ser	ttc Phe	agc Ser	672
cta Leu 225	Thr	ttt Phe	ata Ile	aat Asn	aac Asn 230	Pro	aat Asn	ggt Gly	gaa Glu	gaa Glu 235	Ser	gag Glu	ctg Lev	ctt Lev	tac Tyr 240	720
aag Lys	cct Pro	gca Ala	tca Ser	ctc Leu 245	Gly	aca Thr	ttt Phe	caa Gln	aga Arg 250	, val	gca Ala	cce Pro	gaa Glu	tgg Trp 25!	g atg p Met	768
aga Arg	ı gaa g Glu	gtt Val	ata Ile 260	Lys	ttc Phe	ago Ser	aca Thr	agt Ser 265	Met	g tgt : Cys	cco Pro	c ato	Phe 27	= PIII	t gaa e Glu	816
aga Arg	a gto g Val	tct l Sei 275	Arg	gto y Val	att L Ile	aag E Lys	g cto Lev 280	ı Asr	tgt Cy:	t <b>t</b> ga	a.					849

<210> 58

<211> 282

<212> PRT

<213> Arabidopsis thaliana

<400> 58

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1 5 10 15

Lys Lys Lys Tyr Ser Glu Tyr Asp Glu Ile Asn Lys Glu Gln Glu Glu 20 25 30

Lys Phe Leu Thr Phe Val Ser Ala Ser Glu Glu Leu Met Glu His Leu 35 40 45

Arg Gly Glu Asn Gln Ser Ser Leu Glu Met Val Glu Lys Leu Arg Asn 50 55 60

- Glu Ile Ile Ser Ile Arg Ser Gly Arg Asp Asp Lys Phe Leu Glu Cys
  65 70 75 80
- Gln Lys Leu Leu Met Glu Glu Glu Leu Lys Asn Lys Ser Leu Ser Glu 85 90 95
- Glu Val Val Lys Leu Lys Glu Leu Val Gln Glu Glu His Pro Arg Asn 100 105 110
- Tyr Glu Asp Gln Ser Gly Lys Lys Gln Lys Arg Lys Thr Pro Glu Ser 115 120 125
- Ala Arg Val Thr Thr Arg Ser Met Ile Lys Arg Ser Arg Leu Ser Glu 130 135 140
- Asp Leu Val Glu Thr Asp Met Val Ser Pro Asp Ile Ser Lys His His 145 150 155 160
- Lys Ala Lys Glu Pro Leu Leu Val Ser Gln Pro Gln Cys Cys Arg Thr 165 170 175
- Thr Tyr Asp Gly Ser Ser Ser Ser Ala Ser Cys Thr Phe Gln Ala Leu 180 185 190
- Gly Lys His Leu Leu Gly Met Lys Leu Ser Thr Asn Asn Lys Gly Lys 195 200 205
- Arg Ala Cys Ile Val Ala Ser His Pro Thr Thr Gly Leu Ser Phe Ser 210 215 220
- Leu Thr Phe Ile Asn Asn Pro Asn Gly Glu Glu Ser Glu Leu Leu Tyr 225 230 235 240
- Lys Pro Ala Ser Leu Gly Thr Phe Gln Arg Val Ala Pro Glu Trp Met 245 250 255
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- Arg Val Ser Arg Val Ile Lys Leu Asn Cys 275 280

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155

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gac Asp	aat Asn 210	gga Gly	atg Met	ctt Leu	ccc Pro	atc Ile 215	agt Ser	gtt Val	ctc Leu	ttc Phe	cca Pro 220	tat Tyr	ctc Leu	cca Pro	att Ile	672
cca Pro 225	gct Ala	cac His	cgc Arg	cgt Arg	cgt Arg 230	gac Asp	cgt Arg	gcc Ala	cga Arg	gaa Glu 235	aag Lys	ctt Leu	tcg Ser	gag Glu	att Ile 240	720
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gga Gly	caa Gln 290	His	acg Thr	ago Ser	tct Ser	ato Ile 295	Thi	tcc Ser	acc Thr	tgg Trp	acc Thi	c GTA	gct Ala	tat a Tyr	c ctg	912
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atg Met	gat : Asp	gti Vai	t cto l Leu 340	тут	c cgo	c tgo g Cys	at Il	t aag e Ly: 34!	s Gl	a gc	g tt a Le	g agg	g ct g Le 35	u Hl	c cct s Pro	1056
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gct	c cgg a Arg	g As	t gga p Gl	a aa y Ly	a ac	t tag r Ty: 37	r As	t at p Il	c cc e Pr	a aa o Ly	g gg s Gl 38	у ні	c at s Il	c gt e Va	t gca l Ala	1152
acc Th: 38!	r Se	c cc r Pr	t gc o Al	a tt a Ph	t gc e Al 39	a As	c cg n Ar	c tt g Le	a cc u Pr	g ca o Hi 39	s IJ	c tt le Ph	c aa le Ly	a ga rs As	ec ccc sp Pro 400	)

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tgc Cys	ctt Leu	gga Gly 435	gag Glu	ccg Pro	ttt Phe	gct Ala	tac Tyr 440	ctg Leu	cag Gln	atc Ile	aaa Lys	gcc Ala 445	ata Ile	tgg Trp	agt Ser	1344
cat His	ttg Leu 450	ttg Leu	agg Arg	aac Asn	ttc Phe	gag Glu 455	ctt Leu	gag Glu	cta Leu	gtt Val	tca Ser 460	PLO	ttc Phe	cct Pro	gag Glu	1392
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Leu Val Gly Ser Leu Ile Lys Phe Leu Lys Gly Pro Ile Ile Met Leu 50 55 60

Arg Glu Glu Tyr Pro Lys Leu Gly Ser Val Phe Thr Val Asn Leu Val 65 70 75 80

His Lys Lys Ile Thr Phe Leu Ile Gly Pro Glu Val Ser Ala His Phe 85 90 95

Phe Lys Ala Ser Glu Ser Asp Leu Ser Gln Gln Glu Val Tyr Gln Phe 100 105 110

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- Lys Leu Lys Gly Tyr Val Asp Met Met Val Thr Glu Ala Glu Asp Tyr 145 150 155 160
- Phe Ser Lys Trp Gly Glu Ser Gly Glu Val Asp Ile Lys Val Glu Leu 165 170 175
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- Pro Ala His Arg Arg Arg Asp Arg Ala Arg Glu Lys Leu Ser Glu Ile 225 230 235 240
- Phe Ala Lys Ile Ile Gly Ser Arg Lys Arg Ser Gly Lys Thr Glu Asn 245 250 255
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Met Asp Val Leu Tyr Arg Cys Ile Lys Glu Ala Leu Arg Leu His Pro 340 345

Pro Leu Ile Met Leu Met Arg Ala Ser His Ser Asp Phe Ser Val Thr 355 360 365

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Thr Ser Pro Ala Phe Ala Asn Arg Leu Pro His Ile Phe Lys Asp Pro 385 390 395 400

Asp Thr Tyr Asp Pro Glu Arg Phe Ser Pro Gly Arg Glu Glu Asp Lys 405 410 415

Ala Ala Gly Ala Phe Ser Tyr Ile Ala Phe Gly Gly Gly Arg His Gly 420 425 430

Cys Leu Gly Glu Pro Phe Ala Tyr Leu Gln Ile Lys Ala Ile Trp Ser 435 440 445

His Leu Leu Arg Asn Phe Glu Leu Glu Leu Val Ser Pro Phe Pro Glu 450 455 460

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gga Gly	aaa Lys	cgt Arg	ttt Phe 100	gcc Ala	tgt Cys	gat Asp	gag Glu	ctt Leu 105	tac Tyr	ttg Leu	agt Ser	gat Asp	gaa Glu 110	Ser	gat Asp	336
gaa Glu	gag Glu	ttt Phe 115	gat Asp	cat His	gaa Glu	cct Pro	gag Glu 120	Tyr	atg Met	atg Met	aat Asr	aag Lys 125	Leu	ggt Gly	ctg Leu	384
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cg: Ar	a aaa g Lys	a gtt s Val	Ala	gaa a Gli	a gca u Ala	a ctt a Lei	gat 1 Asj 200	o Thi	c cat	t cto	g ac u Th	t gc r Al 20	a Va	c ca l Gl	a cgc n Arg	624
ga: Gl:	a cat u Hi: 21	s Lys	a att	aaa e Lys	a tog s Sei	g caa Gli 21!	a Il	a gaa e Gli	a gaa u Gl	a ag u Ar	a aa g Ly 22	s Il	a ag e Ar	g ag g Se	c gag r Glu	672
qa	a qc	t cad	g gag	g ga	g gco	c ag	g ag	g aa	g ga	a ag	g go	t ca	t ca	a ga	a gag	720

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aca Thr	acg Thi	g aa c As:	c ca n Gl: 34	a tog n Sei	g ctt r Lei	aag 1 Lys	tca Sei	a cgt c Arg 34!	g Sei	a aat c Ası	ga Gl	a aa u Aa	sn i	tt Phe 350	ago	c a	gt Ser	1056
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gt Va	t ta l Ty	c at	le A	ac to sn Se 20	a ca er Gl	g tt n Ph	t co e Pr	c ca co Gl	ln Va	t at al Me	g g et A	at a sp :	att Ile	ctt Let 430	у пе	eu	gcg Ala	1296
ga Gl	ıa tt .u Pl	ne H	ac a is L 35	aa go ys Al	et t <u>e</u> la Cy	gc at /s Il	t ta e Ty	er Ti	et gt hr Va	al Pi	ca a ro L	ys .	cat His 445	ati Il	t gt e Va	al	aac Asn	1344
to Se	er G	ag t ln S	ca g er A	ct to la T	rp As	at to sp Se	er A	ac g sp A	ca ta la T	at g yr G	Lu P	rgc 160	cta Leu	ga As	t to p So	ct er	ata Ile	1392
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cag ttt ct Gln Phe Le 530	g aag gtt u Lys Val	gtg aat gt Val Asn Va 535	t gtg aga l Val Arg	gag cat ttc. Glu His Phe 1 540	ttg cag aaa 163 Leu Gln Lys	32
ttg cgg gc Leu Arg Al 545	g aag aag a Lys Lys	g gac acg to s Asp Thr Se 550	r Asp Leu	ctt gtg atc Leu Val Ile 555	ata gcc gaa 16 Ile Ala Glu 560	80
atc aca go Ile Thr Al	g tac tta a Tyr Lei 565	ı Asp Asp Ar	g atg tat g Met Tyr 570	ctc aag gaa Leu Lys Glu	cct gaa gga 17 Pro Glu Gly 575	28
aga gct at Arg Ala Me	g aag acg t Lys Thi 580	g act agt ac r Thr Ser Th	c ttg tcc r Leu Ser 585	tct gaa ctt Ser Glu Leu	act gct gaa 17 Thr Ala Glu 590	76
tta aat ca Leu Asn Gl	n Pro Asi	c tac aat ca n Tyr Asn Gl 60	n Asn Tyr	cag agg aat Gln Arg Asn 605	gat tac aga 18 Asp Tyr Arg	24
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- Gly Lys Arg Phe Ala Cys Asp Glu Leu Tyr Leu Ser Asp Glu Ser Asp 100 105 110
- Glu Glu Phe Asp His Glu Pro Glu Tyr Met Met Asn Lys Leu Gly Leu 115 120 125
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- Lys Asp Asp Ile Arg Asn Gln Val Ser Val Val Glu Thr Glu Ile Met 145 150 155 160
- Asn Glu Ile Glu Thr Ser Leu Ser Ala Ile Ala Arg Val Glu Lys Tyr 165 170 175
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- Arg Lys Val Ala Glu Ala Leu Asp Thr His Leu Thr Ala Val Gln Arg 195 200 205
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- Glu Ala Gln Glu Glu Ala Arg Arg Lys Glu Arg Ala His Gln Glu Glu 225 230 235 240
- Lys Ile Arg Gln Glu Lys Ala Arg Ala Glu Ala Gln Met Leu Ala Lys 245 250 255
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- Val Tyr Ile Asn Ser Gln Phe Pro Gln Val Met Asp Ile Leu Leu Ala 420 425 430
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- Met Arg Leu Tyr Gly Ala Leu Val Gln Thr Asp Ile Arg Val Gly Asn 465 470 475 480
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cga Arg	ccc Pro	ctc Leu 35	tta Leu	agc Ser	ttt Phe	tcc Ser	gtc Val 40	aaa Lys	gct Ala	tcc Ser	aga Arg	aag Lys 45	caa Gln	gta Val	gag Glu	144

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gat Asp	tta Leu	gcc Ala	tct Ser	Leu	ttt Phe	cat His	gtg Val	att Ile 105	agc Ser	tta Le	a gga	a ga y As	P 11	nt a	att Ile	aaa Lys	336
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caa Gln	gga Gly 130	Va]	e ect L Pro	gtt Val	gat Asp	999 Gly	Arg	aat Asn	cto Lev	g at	t at e Il 14	e 11)	a g /s A	ca la	ctt Leu	aac Asn	432
ctt Leu 145	Tyr	agg Arg	g aag	g aaa s Lys	a act s Thi 150	gly	agt Ser	aac Asr	aga n Ar	a tt g Ph 15	e Pn	c to	gg a rp I	tt le	cat His	tta Leu 160	480
gat Asp	aaç Lys	g aag E Ly:	g gt s Va	g cc 1 Pro 16	o Th	ggg Gly	gct Ala	gga Gly	a ct 7 Le 17	u G1	t gg y Gl	jt g Ly G	ga a ly s	igt Ser	agt Ser 175	aat Asn	528
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at Il 22	e Va	c ca l Gl	a ga In As	ic ct sp Le	t co eu Pr 23	o Pr	a cc o Pr	t tt	t co ne P:	ro L	tt g eu A 35	at d	ett Leu	ccg Pro	at Me	g gte t Va 24	•
ct Le	c at u Il	a aa .e Ly	ag co ys Pi	ro Ai	ga ga cg G] 15	a go lu Al	a to a Cy	rt to	er T	ct g hr A 50	ct g la G	gaa g Slu	gtt Val	tac Tyr	аа : Ly 25	a cg s Ar 55	t 768 g
ct Le	t cc au Ai	gt ti	eu A	at ca sp Gi	ag ao ln Tl	eg ag ir Se	jc aa er As	sn I.	tt a le A 65	at c	cc t ro I	tg Leu	aca Thr	tta Lei 270	ע דופ	a ga eu Gl	g 816 u
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Ile Val Phe Asp Pro Asp Glu Arg Leu Asn Lys Ile Gly Asp Asp Val 50 55 60

Asp Lys Glu Ala Pro Leu Ser Arg Leu Lys Leu Phe Ser Pro Cys Lys 65 70 75 80

Ile Asn Val Phe Leu Arg Ile Thr Gly Lys Arg Glu Asp Gly Phe His 85 90 95

Asp Leu Ala Ser Leu Phe His Val Ile Ser Leu Gly Asp Thr Ile Lys 100 105 110

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- Gln Gly Val Pro Val Asp Gly Arg Asn Leu Ile Ile Lys Ala Leu Asn 130 135 140
- Leu Tyr Arg Lys Lys Thr Gly Ser Asn Arg Phe Phe Trp Ile His Leu 145 150 155 160
- Asp Lys Lys Val Pro Thr Gly Ala Gly Leu Gly Gly Gly Ser Ser Asn 165 170 175
- Ala Ala Thr Ala Leu Trp Ala Ala Asn Glu Leu Asn Gly Gly Leu Val 180 185 190
- Thr Glu Asn Glu Leu Gln Asp Trp Ser Ser Glu Ile Gly Ser Asp Ile 195 200 205
- Pro Phe Phe Phe Ser His Gly Ala Ala Tyr Cys Thr Gly Arg Gly Glu 210 215 220
- Ile Val Gln Asp Leu Pro Pro Pro Phe Pro Leu Asp Leu Pro Met Val 225 230 235 240
- Leu Ile Lys Pro Arg Glu Ala Cys Ser Thr Ala Glu Val Tyr Lys Arg 245 250 255
- Leu Arg Leu Asp Gln Thr Ser Asn Ile Asn Pro Leu Thr Leu Leu Glu 260 265 270
- Asn Val Thr Ser Asn Gly Val Ser Gln Ser Ile Cys Val Asn Asp Leu 275 280 285
- Glu Pro Pro Ala Phe Ser Val Leu Pro Ser Leu Lys Arg Leu Lys Gln 290 295 300
- Arg Ile Ile Ala Ser Gly Arg Gly Glu Tyr Asp Ala Val Phe Met Ser 305 310 315 320
- Gly Ser Gly Ser Thr Ile Ile Gly Ile Gly Ser Pro Asp Pro Pro Gln 325 330 335

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cca act ttc att gta cgg aaa aga cca gta aag ctc agt tct ctt aac

240

288

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					gaa Glu 150											480
					atc Ile											<b>528</b>
					ttg Leu											576
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	Asp				tgc Cys 230										tct Ser 240	720
					acc Thr										Ala	768
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							Gly					Arg			gly agg	912
	Arg										Ile				gga Gly 320	960
										Arg					g att a Ile	1008
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Asp Val Ala Lys Ala Ile Ser Lys Phe Glu Pro Val Thr Val Cys Ala 50 55 60

Ser Pro Ala Gln Trp Glu Asn Ala Arg Lys Gln Leu Pro Glu Asp Ile 65 70 75 80

Arg Val Val Glu Met Ser Met Asn Asp Ser Trp Phe Arg Asp Ser Gly 85 90 95

Pro Thr Phe Ile Val Arg Lys Arg Pro Val Lys Leu Ser Ser Leu Asn 100 105 110

Arg Asn Ile Ala Gly Ile Asp Trp Asn Phe Asn Ala Trp Gly Gly Ala 115 120 125

Asn Asp Gly Cys Tyr Asn Asp Trp Ser His Asp Leu Leu Val Ser Arg 130 135 140

Lys Ile Leu Ala Leu Glu Arg Ile Pro Arg Phe Gln His Ser Met Ile 145 150 155 160

Leu Glu Gly Gly Ser Ile His Val Asp Gly Glu Gly Thr Cys Leu Val
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Thr Glu Glu Cys Leu Leu Asn Lys Asn Arg Asn Pro His Met Ser Lys
180 185 190

Glu Gln Ile Glu Glu Leu Lys Lys Tyr Leu Gly Val Gln Ser Phe 195 200 205

Ile Trp Leu Pro Arg Gly Leu Tyr Gly Asp Glu Asp Thr Asn Gly His 210 215 220

Ile Asp Asn Met Cys Cys Phe Ala Arg Pro Gly Val Val Leu Leu Ser 225 230 235 240

Trp Thr Asp Asp Glu Thr Asp Pro Gln Tyr Glu Arg Ser Val Glu Ala
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Leu Ser Val Leu Ser Asn Ser Ile Asp Ala Arg Gly Arg Lys Ile Gln 260 265 270

Val Ile Lys Leu Tyr Ile Pro Glu Pro Leu Tyr Met Thr Glu Glu Glu 275 280 285

Ser Ser Gly Ile Thr Gln Asp Gly Glu Ala Ile Pro Arg Leu Ala Gly 290 295 300

Thr Arg Leu Ala Ala Ser Tyr Val Asn Phe Tyr Ile Ala Asn Gly Gly 305 310 315 320

Ile Ile Ala Pro Gln Phe Gly Asp Pro Ile Arg Asp Lys Glu Ala Ile 325 330 335

Arg Val Leu Ser Asp Thr Phe Pro His His Ser Val Val Gly Ile Glu 340 345 350

Asn Ala Arg Glu Ile Val Leu Ala Gly Gly Asn Ile His Cys Ile Thr 355 360 365

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PCT/EP02/07929 WO 03/008440

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cat His	tgg Trp	gga Gly	gga Gly 100	Phe	gac Asp	cct Pro	cta Leu	tca Ser 105	Ser	atg Met	aat Asn	gcg Ala	aag Lys 110	Pro	gtt Val	336
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tcc Ser 145	: Ile	aat Asr	ttt Phe	: cta : Lev	gaa Glu 150	Ser	tco Sei	c act	t toa	a tat r Tyi 159	c Als	gct A Ala	cct a Pro	ac Th	a tgg r Trp 160	480

145

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G1 39	a ag y Se 37	r Gl	g aad y Asi	e gaa n Glu	a aga u Arg	a gg g Gl; 37	y Al	a ata a Il	a gc e Al	c at a Il	c tt e Le 38	u Le	a aa u Ly	a gc s Al	g aca a Thr	1152
ga G1 38	u Se	t ca r Gl	g gag n Gl	g aag u Lys	g tta s Le 39	u Se	a gg r Gl	c ag y Ar	a ga g As	t ct p Le 39	u Th	t aa Ir As	t gg n Gl	c ca y Gl	a tgt n Cys 400	

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Tyr Tyr His '	act cta cas Thr Leu Glr 420	a atc ttt gtg n Ile Phe Val 425	gat caa caa cag aag aca gac Asp Gln Gln Gln Lys Thr Asp 430	1296
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PCT/EP02/07929 WO 03/008440

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Gly Val Glu Leu Trp Ala Val Phe Asp Val Pro Gln Ser Gln Val Asp 120 115

Thr Ser Trp Lys Asn Leu Thr His Ala Leu Ser Gly Leu Phe Cys Ala 135 130

Ser Ile Asn Phe Leu Glu Ser Ser Thr Ser Tyr Ala Ala Pro Thr Trp 155 145 150

Gly Phe Gly Pro Asn Ser Asp Lys Leu Arg Tyr Gly Ser Leu Pro Arg 170 165

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- Ile Arg Glu Ser Cys Ser Phe Leu Phe Ile Phe Asp Ile Asp Lys Ser 325 330 335
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- Lys Trp Ser Cys Gln Gln Ala Pro Leu His Ser Ser Arg Phe Leu Met 355 360 365
- Gly Ser Gly Asn Glu Arg Gly Ala Ile Ala Ile Leu Leu Lys Ala Thr 370 375 380
- Glu Ser Gln Glu Lys Leu Ser Gly Arg Asp Leu Thr Asn Gly Gln Cys 385 390 395 400
- Thr Ile Lys Ala Asn Ile Phe Gln Ile Phe Pro Trp Tyr Ile Lys Val 405 410 415

Tyr Tyr His Thr Leu Gln Ile Phe Val Asp Gln Gln Gln Lys Thr Asp 420 425 430

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Ser Val Ala Ile Ser Ile Glu Tyr Asp Lys Gly Phe Leu His Ile Asp 465 470 475 480

Glu Tyr Pro Pro Asp Ala Asn Gln Gly Phe Asp Ile Pro Ser Ala Leu 485 490 495

Ile Ser Phe Pro Asp His His Ala Ser Leu Asp Phe Gln Glu Glu Leu 500 505 510

Ser Asn Ser Pro Leu Leu Ser Ser Leu Lys Glu Lys Ser Leu Val Arg 515 520 525

Ser Tyr Thr Glu Val Leu Leu Val Pro Leu Thr Thr Pro Asp Phe Ser 530 535 540

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Leu Leu Ser Arg Ile Thr Ala Lys Ile Arg Gly Arg Pro Ile Glu Ala 595 600 605

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95

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ccg	cct Pro	gg Gl	a aa y As 18	n Va	a tat l Ty	gca Ala	a ato	c aad e Asi 18!	1 GT	a gco u Ala	c cto	c tco u Se:	c gct r Ala 190		g g u A	ıct . Ma	576
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ati Ile	t ct e Le 21	u Ar	t gt g Va	a to	t ga r Gl	a tc u Se 21	r Tn	t gg r Gl	c tt y Ph	t cc e Pr	с аа о <b>L</b> y 22	a tt rs Ph	t ga le As	t ct p Le	c a	atg Met	672
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to Se	t co	ca aa co Ly	ys P	ca c ro P	cg to ro Se	et ga er Gl	ig aç lu Ai	cg 1.	c a le T	cc ti hr Pl	cc a he T	cg t hr P	ne r	eg g ro V 70	tc al	atc Ile	816
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G	gt t ly S 05	ct g er V	tt t	ct g er <i>F</i>	la G	aa g lu A 10	ac g sp G	ag t	tg g eu V	aı ı	gg trp I	ctc o	etg g Seu A	ac :	aaa Lys	cca Pro 320	960
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Val Ser Ser Ile Gly Thr Gly Ser Thr Lys Lys Ser Ser Asp Thr Arg 50 55 60

Arg Lys Val Lys Ser Met Ala Thr Thr Asn Ile Gly Lys Glu Glu Lys 65 70 75 80

Lys Arg Val Glu Ile Tyr Asp Leu Glu Glu Asn Leu Val Ile Asp Leu 85 90 95

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Ala Phe Thr Val Val Val Ser Gly Gly Ser Leu Ile Lys Ser Leu Arg 115 120 125

Lys Leu Val Glu Ser Pro Tyr Val Asp Ser Ile Asp Trp Ala Arg Trp 130 135 140

His Phe Phe Trp Val Asp Glu Arg Val Val Pro Lys Asn His Asp Asp 145 150 155 160

Ser Asn Tyr Lys Leu Ala Tyr Asp Ser Phe Leu Ser Lys Val Pro Ile 165 170 175

Pro Pro Gly Asn Val Tyr Ala Ile Asn Glu Ala Leu Ser Ala Glu Ala 180 185 190

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Leu Leu Gly Met Gly Pro Asp Gly His Val Ala Ser Leu Phe Pro Gly 225 230 235 240

His Gly Leu Cys Asn Glu Ser Lys Lys Trp Val Val Ser Ile Ser Asp 245 250 255

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ttt Phe	ctc Leu	cca Pro 35	cac His	ggc Gly	ggc Gly	gct Ala	tta Leu 40	aga Arg	acc Thr	ggc	gt Va	Τ 2	cg Ser 15	tgt Cys	agc Ser	to T:	г <b>р</b> 33		144
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age ceg gee gag ete ggg aac aag ata tat gag atg atg gea atg geg	2208

Ser Pro Ala Glu Leu Gly Asn Lys Ile Tyr Glu Met Met Ala Met Ala 725 730 735

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gtg aat gaa gga gat gac aaa agc gga gaa aca gag gta gtt gaa cca 2304 Val Asn Glu Gly Asp Asp Lys Ser Gly Glu Thr Glu Val Val Glu Pro 755 760 765

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Tyr Ser His Lys Glu Val Phe Leu Arg Glu Leu Val Ser Asn Ala Ser 100 105 110

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Asn Gly Thr Ile Thr Ile Thr Asp Thr Gly Ile Gly Met Thr Lys Glu 145 150 155 160

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Phe Leu Lys Ala Leu Lys Glu Asn Lys Asp Leu Gly Ala Asp Asn Gly 180 185 190

Leu Ile Gly Gln Phe Gly Val Gly Phe Tyr Ser Ala Phe Leu Val Ala 195 200 205

Glu Lys Val Val Val Ser Thr Lys Ser Pro Lys Ser Asp Lys Gln Tyr 210 215 220

Val Trp Glu Ser Val Ala Asp Ser Ser Ser Tyr Leu Ile Arg Glu Glu 225 230 235 240

Thr Asp Pro Asp Asn Ile Leu Arg Arg Gly Thr Gln Ile Thr Leu Tyr 245 250 255

Leu Arg Glu Asp Asp Lys Tyr Glu Phe Ala Glu Ser Thr Arg Ile Lys 260 265 270

Asn Leu Val Lys Asn Tyr Ser Gln Phe Val Gly Phe Pro Ile Tyr Thr

Trp Gln Glu Lys Ser Arg Thr Ile Glu Val Glu Glu Asp Glu Pro Val 290 295 300

Lys Glu Gly Glu Gly Glu Pro Lys Lys Lys Lys Thr Thr Lys Thr 305 310 315

Glu Lys Tyr Trp Asp Trp Glu Leu Ala Asn Glu Thr Lys Pro Leu Trp 325 330 335

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Glu Leu Phe Pro Arg Tyr Leu Ser Phe Val Lys Gly Val Val Asp Ser 420 425 430

Asp Asp Leu Pro Leu Asn Val Ser Arg Glu Ile Leu Gln Glu Ser Arg 435 440 445

Ile Val Arg Ile Met Arg Lys Arg Leu Ile Arg Lys Thr Phe Asp Met 450 455

Ile Gln Glu Ile Ser Glu Ser Glu Asn Lys Glu Asp Tyr Lys Lys Phe 465 470 475 480

Trp Glu Asn Phe Gly Arg Phe Leu Lys Leu Gly Cys Ile Glu Asp Thr 485 490 490

Gly Asn His Lys Arg Ile Thr Pro Leu Leu Arg Phe Phe Ser Ser Lys 500 505 510

Asn Glu Glu Glu Leu Thr Ser Leu Asp Asp Tyr Ile Glu Asn Met Gly 515 520 525

Glu Asn Gln Lys Ala Ile Tyr Tyr Leu Ala Thr Asp Ser Leu Lys Ser 530 535 540

Ala Lys Ser Ala Pro Phe Leu Glu Lys Leu Ile Gln Lys Asp Ile Glu 545 550 555 560

Val Leu Tyr Leu Val Glu Pro Ile Asp Glu Val Ala Ile Gln Asn Leu 565 570 575

Gln Thr Tyr Lys Glu Lys Lys Phe Val Asp Ile Ser Lys Glu Asp Leu 580 585 590

Glu Leu Gly Asp Glu Asp Glu Val Lys Asp Arg Glu Ala Lys Gln Glu
595 600 605

Phe Asn Leu Leu Cys Asp Trp Ile Lys Gln Gln Leu Gly Asp Lys Val 610 615 620

Ala Lys Val Gln Val Ser Asn Arg Leu Ser Ser Ser Pro Cys Val Leu 625 630 635 640

Val Ser Gly Lys Phe Gly Trp Ser Ala Asn Met Glu Arg Leu Met Lys 645 650 655

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gt Va	c ca l Hi	t gg s Gl	y Ar	g tt g Le	g ag u Se	t gg r Gl	g at y Il 20	e G	a ca lu Hi	at ga is Aa	at g sp G	TA.	aac Asr 205	1 11	a ti e L	tg eu	ttt Phe	624	;
to Se	r As	at at sp I] 10	t co e Pr	a to o Se	c gg r Gl	g ag y Ar 21	g As	nc to sn Se	et ga er A	at t sp P	ne i	ag ys 220	gtt Va]	; gt L Va	t a al A	ga rg	tac Tyr	672	2

1	cat His 225	tca Ser	ctg Leu	atc Ile	ata Ile	gat Asp 230	aag Lys	gaa Glu	tca Ser	cta Leu	cca Pro 235	aag Lys	gaa Glu	ctt Leu	gta Val	. P.	ca ro 40	72	20
•	ata Ile	gcg Ala	tgg Trp	acg Thr	att Ile 245	tat Tyr	gat Asp	gac Asp	act Thr	ggc Gly 250	tct Ser	ttc Phe	tct Ser	gag Glu	aag Lys 255	A	at sn	7(	58
	tcc Ser	tgt Cys	gtt Val	cct Pro 260	gtg Val	aat Asn	aac Asn	act Thr	999 Gly 265	agc Ser	cca Pro	ctt Leu	ejy aaa	aac Asn 270	GTZ	a t	ct Ser	8	16
	gtc Val	att Ile	cct Pro 275	Val	tca Ser	gaa Glu	aag Lys	tta Leu 280	gaa Glu	aat Asn	cga Arg	agt Ser	cat His 285	urp	Pre	t t	cg Ser	8	64
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	cat His 305	Ser	tct Ser	ttt Phe	ccc Pro	cat His	Tyr	ggt Gly	tta Leu	cag Gln	ttt Phe 315	HIS	cca Pro	gaa Glu	ag 1 Se	T.	att Ile 320		60
	gct Ala	act Thr	acc Thi	tat Tyr	ggt Gly 325	agt Ser	cag Gln	tta Leu	ttt Phe	aaa Lys 330	Asn	tto Phe	aaq E Ly:	g gad s Ası	at o Il 33	.e	act Thr	10	800
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	ata Ile	a aat e Asr	gae Asj 35	o Th	gca c Ala	a aad a Asi	ato Met	g cag Glr 360	ı Va.	g cct l Pro	gat Asj	o Al	t ac a Th 36	r GI	a ti n Le	eu	ctg Leu	1	104
	aaa Lys	a gaa s Glu 370	ı Le	t tc u Se	t aga	a act	aga r Arg 37!	g Cy	t aca	a gg r Gl	a aat y Asi	t gg n Gl 38	у ѕе	t ag r Se	c to	at yr	ttt Phe	. 1	152
	gg: 38:	y Ası	c cc n Pr	t aa o Ly	g tc s Se	t ctg r Le 39	u Ph	t tc e Se	t gc r Al	c aa a Ly	g ac s Th 39	r As	t gg n Gl	ıt gt .y Va	ag lA	ac sp	gtc Val 400	1	.200
	tt Ph	t ga e As	t at p Me	g gt t Va	g ga 1 As 40	t tc p Se 5	a tc r Se	a ta r Ty	t cc r Pr	a aa o Ly 41	s Pr	a ca o Hi	t ac	a aa r by	'S L	tg eu 15	пеп	1	L248
	ag Ar	g tt g Le	g aa u Ly	a tg s Tr 42	р га	g aa s Ly	g ca s Hi	t ga s Gl	a cg u Ar 42	g Le	t go u Al	g ca .a Hi	at aa is Ly	ys va	al G	gt ly	gga Gly	:	1296
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	ac Th	et tt ir Ph 45	e Ti	gg ct cp Le	g ga eu As	t ac sp Th	t to r Se 45	er Se	et ag er Se	gt ga er A	ac aa sp Ly	ys A	ct a la A 60	ga g rg G	ga o ly 1	arç	ttt g Phe		1392

tct Ser 465	ttc Phe	atg Met	ggc	Gly	aaa Lys 470	ggt Gly	gga Gly	tct Ser	Leu	tgg Trp 475	aag Lys	caa Gln	ttg Leu	a a	nr .	ttt Phe 480	1440
agt Ser	tta Leu	tct Ser	gat Asp	caa Gln 485	agt Ser	gag Glu	gtt Val	Thr	tca Ser 490	aaa Lys	cat His	gcg Ala	gga	, н	at is 95	ctt Leu	1488
ctg Leu	att Ile	gaa Glu	gat Asp 500	tct Ser	cag Gln	agt Ser	tct Ser	act Thr 505	gag Glu	aaa Lys	caa Gln	ttc Phe	Let 51	a G	gaa Slu	gaa Glu	1536
ggc Gly	ttt Phe	ctt Leu 515	gat Asp	ttt Phe	ctc Leu	cgt Arg	aag Lys 520	gag Glu	ctt Leu	tca Ser	tct Ser	ato Ile 525	. Se	t t	tat Tyr	gat Asp	1584
gag Glu	aag Lys 530	gac Asp	ttc Phe	gaa Glu	gag Glu	ttg Leu 535	cct Pro	ttt Phe	gat Asp	ttt Phe	tgc Cys 540	GT?	gg Gl	a t y ?	cac Tyr	gta Val	1632
ggt Gly 545	tgt Cys	att Ile	gly aaa	tat Tyr	gat Asp 550	att Ile	aaa Lys	gtg Val	gaa Glu	tgt Cys 555	GTA	ato Mei	g cc E Pr	a a	att Ile	aat Asn 560	1680
cgt Arg	cac His	aaa Lys	tcc Ser	aac Asn 565	gct Ala	cca Pro	gat Asp	gca Ala	tgt Cys 570	Phe	tto Phe	e tt	t go e Al	La .	gat Asp 575	ASI	1728
gtt Val	gtc Val	gcc Ala	att Ile 580		cat His	caa Gln	ctc Leu	gat Asp 585	Asp	gtt Val	tai L Ty:	t at r Il	е те	eu 90	tcg Ser	ctt Leu	1776
tac Tyr	gaa Glu	gag Glu 595	Gly	act Thr	gca Ala	gaa Glu	acc Thr 600	Ser	tto Phe	ct <u>e</u> Lev	g aa 1 As	t ga n As 60	рт	ct hr	gaa Glu	gag Glu	1824
aa <u>c</u> Lys	cto Lev 610	Ile	ago Ser	ttg Lev	atg Met	ggt Gly 615	Leu	g tco 1 Ser	aca Thi	a aga	a aa g <b>L</b> y 62	s re	g g u G	ag lu	gat	caa Gln	1872
act Thi 625	Lev	cca Pro	a gtt o Val	ata L Ile	gat Asp 630	Se ₁	tct Sei	caa c Glr	a tco n Se	c aa r Ly 63	s Th	a ag ir Se	gt t er P	tt he	gti Va:	cct Pro 640	1920
ga Asj	c aaa o Lys	tco Ser	e ega r Arg	a gag g Gli 64!	ı Glı	g tat n Tyn	t ato	c aad e Ası	c ga n As 65	p Va	t ca 1 Gl	ig ag In Se	gc t er C	gt 'ys	ate Me 65	g aag t Lys 5	1968
ta Ty:	t ato	e aaa	a gad s Asj 66	b GJ	g gaq y Gli	g ago u Se:	c ta r Ty	c gag r Gl	u Le	t tg u Cy	jt ct /s Le	cca eu T	nr 1	ct hr	GT	a aac n Asn	2016
ag Ar	a ag g Ar	g aa g Ly 67	s Il	a gg e Gl	a aa y As:	t gc n Al	t ga a As 68	p Pr	t tt o Le	g gg u G]	ja ci ly L	eu T	at o yr 1 85	ctc Leu	ca Hi	c ctg s Leu	2064
ag Ar	a ga g Gl 69	u Ar	g aa g As	t cc n Pr	a gc o Al	a cc a Pr 69	о Ту	t go r Al	a go a Al	a ti la Pl	ne L	tc a eu A 00	ac sn	ttc Phe	tc Se	a aat er Asn	2112

gca Ala 705	aat Asn	ctg Leu	tct Ser	tta Leu	tgc Cys 710	tct Ser	tcg Ser	tcc Ser	cct Pro	gaa Glu 715	agg Arg	ttt Phe	ctt Leu	aag Lys	ctg Leu 720	2160
gac Asp	aga Arg	aat Asn	gga Gly	atg Met 725	ctt Leu	gaa Glu	gca Ala	aag Lys	ccg Pro 730	att Ile	aag Lys	ggt Gly	act Thr	ata Ile 735	gct Ala	2208
cgt Arg	ggc	tcc Ser	acg Thr 740	cct Pro	gaa Glu	gaa Glu	gat Asp	gaa Glu 745	ttt Phe	ctt Leu	aaa Lys	ttg Leu	caa Gln 750	ttg Leu	aaa Lys	2256
ctc Leu	agt Ser	gag Glu 755	aag Lys	aat Asn	caa Gln	gcc Ala	gag Glu 760	aat Asn	ctg Leu	atg Met	att Ile	gtt Val 765	gac Asp	ctt Leu	cta Leu	2304
agg Arg	aat Asn 770	gat Asp	ctc Leu	ggt Gly	cgt Arg	gtc Val 775	tgt Cys	gag Glu	cct Pro	ggc Gly	tca Ser 780	gtc Val	cat His	gta Val	cct Pro	2352
aac Asn 785	ctc Leu	atg Met	gat Asp	gta Val	gaa Glu 790	tca Ser	tac Tyr	aca	aca Thr	gta Val 795	cat His	aca Thr	atg Met	gtg Val	agc Ser 800	2400
acg Thr	atc Ile	cgt Arg	gga Gly	ctg Leu 805	aaa Lys	aaa Lys	aca Thr	gat Asp	att Ile 810	Ser	cca Pro	gtg Val	gaa Glu	tgt Cys 815	Val	2448
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Ser	Val	Glu 835	Ile	Leu	Asp	Ser	Leu 840	Glu	. Asn	. Cys	Ser	845	Gly	. Lev	tac Tyr	2544
Ser	6ly 850	Ser	Ile	Gly	Тух	855	Ser	Tyr	Asr	ı Gly	860	Phe	e Asr	) Lev	aat 1 Asn	2592
Ile 865	val	Ile	Arg	Thr	* Val 870	. Ile	: Ile	e His	: Glı	1 Asp 875	Glu G	ı Ala	a Sei	r Ile	gga Gly 880	2640
gca	a gga	gga Gly	gct Ala	att Ile 885	· Val	gca Ala	tta Lei	a tca 1 Sei	a agt Sei 890	r Pro	a gaa	a gat u Asj	gag Gli	y tt u Pho 89	t gag e Glu 5	2688
gaa Glu	a at <u>c</u> 1 Met	att : Ile	ctt Lev 900	Lys	g act	aga Arg	a gci g Ala	e cct a Pro 90!	o Ala	t aat a Asi	t gc n Al	a gt a Va	c ate 1 Me 91	f GT	g ttt u Phe	2736
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Pro Lys Trp Lys Lys Ser Phe Ile Ser Leu Pro Cys Arg Ser Lys Thr 35 40 45

Thr Arg Lys Val Leu Ala Ser Ser Arg Tyr Val Pro Gly Lys Leu Glu 50 55

Asp Leu Ser Val Val Lys Lys Ser Leu Pro Arg Arg Glu Pro Val Glu 65 70 75 80

Lys Leu Gly Phe Val Arg Thr Leu Leu Ile Asp Asn Tyr Asp Ser Tyr 85 90 95

Thr Phe Asn Ile Tyr Gln Ala Leu Ser Thr Ile Asn Gly Val Pro Pro 100 105 110

Val Val Ile Arg Asn Asp Glu Trp Thr Trp Glu Glu Ala Tyr His Tyr 115 120 125

Leu Tyr Glu Asp Val Ala Phe Asp Asn Ile Val Ile Ser Pro Gly Pro 130 135 140

Gly Ser Pro Met Cys Pro Ala Asp Ile Gly Ile Cys Leu Arg Leu Leu 145 150 155 160

Leu Glu Cys Arg Asp Ile Pro Ile Leu Gly Val Cys Leu Gly His Gln
165 170 175

Ala Leu Gly Tyr Val His Gly Ala His Val Val His Ala Pro Glu Pro 180 185 190

Val His Gly Arg Leu Ser Gly Ile Glu His Asp Gly Asn Ile Leu Phe 195 200 205

Ser Asp Ile Pro Ser Gly Arg Asn Ser Asp Phe Lys Val Val Arg Tyr 210 215 220

His Ser Leu Ile Ile Asp Lys Glu Ser Leu Pro Lys Glu Leu Val Pro 225 230 235 240

Ile Ala Trp Thr Ile Tyr Asp Asp Thr Gly Ser Phe Ser Glu Lys Asn 245 250 255

Ser Cys Val Pro Val Asn Asn Thr Gly Ser Pro Leu Gly Asn Gly Ser 260 265 270

Val Ile Pro Val Ser Glu Lys Leu Glu Asn Arg Ser His Trp Pro Ser 275 280 285

Ser His Val Asn Gly Lys Gln Asp Arg His Ile Leu Met Gly Ile Met 290 295 300

His Ser Ser Phe Pro His Tyr Gly Leu Gln Phe His Pro Glu Ser Ile 305 310 315 320

Ala Thr Thr Tyr Gly Ser Gln Leu Phe Lys Asn Phe Lys Asp Ile Thr 325 330 335

Val Asn Tyr Trp Ser Arg Cys Lys Ser Thr Ser Leu Arg Arg Arg Asn 340 345 350

Ile Asn Asp Thr Ala Asn Met Gln Val Pro Asp Ala Thr Gln Leu Leu 355 360 365

Lys Glu Leu Ser Arg Thr Arg Cys Thr Gly Asn Gly Ser Ser Tyr Phe 370 375 380

Gly Asn Pro Lys Ser Leu Phe Ser Ala Lys Thr Asn Gly Val Asp Val 385 390 395

Phe Asp Met Val Asp Ser Ser Tyr Pro Lys Pro His Thr Lys Leu Leu 405 410 415

Arg Leu Lys Trp Lys Lys His Glu Arg Leu Ala His Lys Val Gly Gly 420 425 430

Val Arg Asn Ile Phe Met Glu Leu Phe Gly Lys Asn Arg Gly Asn Asp 435 440 445

Thr Phe Trp Leu Asp Thr Ser Ser Ser Asp Lys Ala Arg Gly Arg Phe 450 455 460

Ser Phe Met Gly Gly Lys Gly Gly Ser Leu Trp Lys Gln Leu Thr Phe 465 470 475 480

Ser Leu Ser Asp Gln Ser Glu Val Thr Ser Lys His Ala Gly His Leu 485 490 495

Leu Ile Glu Asp Ser Gln Ser Ser Thr Glu Lys Gln Phe Leu Glu Glu 500 505 510

Gly Phe Leu Asp Phe Leu Arg Lys Glu Leu Ser Ser Ile Ser Tyr Asp 515 520 525

Glu Lys Asp Phe Glu Glu Leu Pro Phe Asp Phe Cys Gly Gly Tyr Val 530 535 540

Gly Cys Ile Gly Tyr Asp Ile Lys Val Glu Cys Gly Met Pro Ile Asn 545 550 555 560

Arg His Lys Ser Asn Ala Pro Asp Ala Cys Phe Phe Phe Ala Asp Asn 565 570 575

Val Val Ala Ile Asp His Gln Leu Asp Asp Val Tyr Ile Leu Ser Leu 580 585 590

Tyr Glu Glu Gly Thr Ala Glu Thr Ser Phe Leu Asn Asp Thr Glu Glu 595 600 605

Lys Leu Ile Ser Leu Met Gly Leu Ser Thr Arg Lys Leu Glu Asp Gln 610 615 620

Thr Leu Pro Val Ile Asp Ser Ser Gln Ser Lys Thr Ser Phe Val Pro 625 630 635 640

Asp Lys Ser Arg Glu Gln Tyr Ile Asn Asp Val Gln Ser Cys Met Lys 645 650 655

Tyr Ile Lys Asp Gly Glu Ser Tyr Glu Leu Cys Leu Thr Thr Gln Asn 660 665 670

Arg Arg Lys Ile Gly Asn Ala Asp Pro Leu Gly Leu Tyr Leu His Leu 675 680 685

Arg Glu Arg Asn Pro Ala Pro Tyr Ala Ala Phe Leu Asn Phe Ser Asn 690 695 700

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Asp Arg Asn Gly Met Leu Glu Ala Lys Pro Ile Lys Gly Thr Ile Ala 725 730 735

Arg Gly Ser Thr Pro Glu Glu Asp Glu Phe Leu Lys Leu Gln Leu Lys 740 745 750

Leu Ser Glu Lys Asn Gln Ala Glu Asn Leu Met Ile Val Asp Leu Leu 755 760 765

Arg Asn Asp Leu Gly Arg Val Cys Glu Pro Gly Ser Val His Val Pro 770 780

Asn Leu Met Asp Val Glu Ser Tyr Thr Thr Val His Thr Met Val Ser 785 790 795 800

Thr Ile Arg Gly Leu Lys Lys Thr Asp Ile Ser Pro Val Glu Cys Val 805 810 815

Arg Ala Ala Phe Pro Gly Gly Ser Met Thr Gly Ala Pro Lys Leu Arg 820 825 830

Ser Val Glu Ile Leu Asp Ser Leu Glu Asn Cys Ser Arg Gly Leu Tyr 835 840 845

Ser Gly Ser Ile Gly Tyr Phe Ser Tyr Asn Gly Thr Phe Asp Leu Asn 850 860

Ile Val Ile Arg Thr Val Ile Ile His Glu Asp Glu Ala Ser Ile Gly 865 870 875 880

Ala Gly Gly Ala Ile Val Ala Leu Ser Ser Pro Glu Asp Glu Phe Glu 885 890 895

Glu Met Ile Leu Lys Thr Arg Ala Pro Ala Asn Ala Val Met Glu Phe 900 905 910

Cys Ser Asp Gln Arg Arg Gln 915

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480

gca aaa act gag aaa att gca ttt atc ctt gaa caa gtt cgc ttg tgc

130

Ala 145	Lys	Thr	Glu	Lys	Ile 150	Ala	Phe	Ile	Leu	Glu 155	Gln	Val	Arg	Leu	10	é0 As		
ttg Leu	gat Asp	cgt Arg	caa Gln	gat Asp 165	ttt Phe	gtt Val	cgt Arg	gca Ala	caa Gln 170	atc Ile	tta Leu	tct Ser	agg Arg	aag Lys 175	, <u>T</u>	tc le	528	
aat Asn	cct Pro	aga Arg	gtt Val 180	ttt Phe	gac Asp	gca Ala	gat ' Asp	aca Thr 185	aaa Lys	aaa Lys	gat Asp	aag Lys	aag Lys 190	. пå:	a c	ro	576	
aag Lys	gaa Glu	ggt Gly 195	Asp	aac Asn	atg Met	gta Val	gaa Glu 200	gag Glu	gct Ala	cct Pro	gct Ala	gat Asp 205	110	e Pr	a a	cc hr	624	
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tat Tyr	gat Asp	ato	cct Pro	tca Ser 245	Val	aaa Lys	gaa Glu	act Thr	ccg Pro 250	gag Glu	caç Gli	g tgg n Trj	g at p Il	t co e Pr 25	.0	gtc Val	768	
ctg Lev	agg Arg	g aag g Ly:	g ato s Ile 260	Cys	tgg Trp	ttc Phe	tt <u>c</u> Leu	gto Val	Leu	gca LAla	. cct	t ca	t ga s As 27	b b	ca co	atg Met	. 816	
caa Glr	a tca 1 Se:	a age r Se: 27:	r Lei	g cto 1 Lei	aat 1 Asr	gca Ala	act Thi	. Lei	g gaa ı Glu	a gac ı Asp	aa Ly	g aa s As 28	п те	a to eu So	ca er	gaa Glu	864	
ato Ile	c cc e Pr	o As	t tt p Ph	e aag	g ato	g ctt Lev 295	ı Leı	a aaa 1 Ly:	a cag s Gli	g gta n Val	a gt L Va 30	T III	a at r Me	g g et G	ag lu	gtt Val	912	
at Il	e Gl	a tg n Tr	g ac p Th	a tc r Se:	t cto r Leo 31	u Trj	g aao o Asi	c aa n Ly	a tao s Ty:	c aag r Lys 31!	s As	t ga p Gl	ig ti lu Pl	tc g ne G	ag lu	aaa Lys 320	960	
ga Gl	g aa u Ly	a ag s Se	c at r Me	g at t Il 32	e Gl	a gg ¹ y Gl ₂	t tc y Se	t tt r Le	g gg u Gl 33	t ga y As 0	c aa p Ly	a go 7s A.	et g la G	TA G	aa lu 35	gat Asp	1008	
ct Le	g aa u Ly	a ct 's Le	g ag u Ar 34	g Il	c at e Il	c ga e Gl	a ca u Hi	t aa s As 34	n II	c ct e Le	c gt u Va	al V	ar o	ca a er I 50	ys	tac Tyr	1056	
ta Ty	ic go r Al	la Ai	gg at cg II	a ac e Tb	c tt r Le	a aa u Ly	g ag s Ar 36	g re	t go eu Al	c ga la Gl	g c	eu b	ta t eu C 65	gc (	ctg Leu	agc Ser	1104	:
at Me	et G	ag ga lu Gi 70	ag go lu Al	g ga La Gl	ig aa lu Ly	ıg ca rs Hi 37	s Le	a to eu Se	eg ga er Gl	ag at lu Me	ec v	ta g al V 80	tg t	ca : Ser :	aaa Lys	gca Ala	1152	?
ct	tg a	tt g	ca a	aa at	a ga	ac aç	ja co	ca t		ga at	t g	tg t	gc 1	ttc	caç	g atc	1200	3

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aag ctt Lys Leu	Leu A	at ctt sp Leu 20	gtg Val	gaa Glu	aag Lys	agt Ser 425	tgc Cys	cac His	caa Gln	att Ile	cac His 430	aag Lys	gaa Glu	1296
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Leu Leu Asn Glu Gln Ile Leu Asn Leu Ser Lys Lys Arg Gly Gln Leu 50 55 60

Lys Gln Ala Val Gln Ser Met Val Gln Gln Ala Met Gln Tyr Ile Asp 65 70 75 80

Gln Thr Pro Asp Ile Glu Thr Arg Ile Glu Leu Ile Lys Thr Leu Asn 85 90 95

Asn Val Ser Ala Gly Lys Ile Tyr Val Glu Ile Glu Arg Ala Arg Leu 100 105 110

Thr Lys Lys Leu Ala Lys Ile Lys Glu Glu Gln Gly Gln Ile Ala Glu 115 120 125

Ala Ala Asp Leu Met Gln Glu Val Ala Val Glu Thr Phe Gly Ala Met 130 135 140

Ala Lys Thr Glu Lys Ile Ala Phe Ile Leu Glu Gln Val Arg Leu Cys 145 150 155 160

Leu Asp Arg Gln Asp Phe Val Arg Ala Gln Ile Leu Ser Arg Lys Ile 165 170 175

Asn Pro Arg Val Phe Asp Ala Asp Thr Lys Lys Asp Lys Lys Pro 180 185 190

Lys Glu Gly Asp Asn Met Val Glu Glu Ala Pro Ala Asp Ile Pro Thr 195 200 205

Leu Leu Glu Leu Lys Arg Ile Tyr Tyr Glu Leu Met Ile Arg Tyr Tyr 210 215 220

Ser His Asn Asn Glu Tyr Ile Glu Ile Cys Arg Ser Tyr Lys Ala Ile 225 230 235 240

Tyr Asp Ile Pro Ser Val Lys Glu Thr Pro Glu Gln Trp Ile Pro Val 245 250 255

Leu Arg Lys Ile Cys Trp Phe Leu Val Leu Ala Pro His Asp Pro Met 260 265 270

Gln Ser Ser Leu Leu Asn Ala Thr Leu Glu Asp Lys Asn Leu Ser Glu 275 280 285

Ile Pro Asp Phe Lys Met Leu Leu Lys Gln Val Val Thr Met Glu Val 290 295 300

Ile Gln Trp Thr Ser Leu Trp Asn Lys Tyr Lys Asp Glu Phe Glu Lys 305 310 315

Glu Lys Ser Met Ile Gly Gly Ser Leu Gly Asp Lys Ala Gly Glu Asp 325 330 335

Leu Lys Leu Arg Ile Ile Glu His Asn Ile Leu Val Val Ser Lys Tyr 340 345 350

Tyr Ala Arg Ile Thr Leu Lys Arg Leu Ala Glu Leu Leu Cys Leu Ser

Met Glu Glu Ala Glu Lys His Leu Ser Glu Met Val Val Ser Lys Ala 370 375 380

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<223> 60944

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PCT/EP02/07929 WO 03/008440

432

435

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tcg Ser	gct Ala	ttg Leu	atg Met 100	gtt Val	gat Asp	gct Ala	gat Asp	caa g Gln ' 105	gtt Val	gag Glu	aag Lys	ttt Phe	cgt Arg 110	пĀг	ag Ar	g .g	3:	36
ttc Phe	gct Ala	ggg Gly 115	ctt Leu	tct Ser	gag Glu	att Ile	atg Met 120	gag Glu	att Ile	cct Pro	gtg Val	ctt Leu 125	гуя	Gly gga	a ga / Gi	aa lu	3	84
atc Ile	att Ile 130	atg Met	cct Pro	act Thr	aag Lys	aaa Lys 135	agt Ser	aaa Lys	ggt Gly	ccc Pro	aaa Lys 140	GTA	aag Lys	g aag Eys	g a	aa ys	4	32
tga															. (		4	35
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Met 1	: Ala	a Val	l Sei	c Leu 5	Pro	Ası	ser	Phe	Leu 10	Gli	ı Il	e Se	r Pr	0 Cy 15	rs ! S	/al		
Pro	Sei	r Lei	1 Gl1 20		ı Arç	j Ly:	e Pro	Val 25	Met	: Al	a Al	a Va	1 Ly 30	rs G] )	Ly (	Gly		
Ly	s Gl	n Se:	r Va	l Arg	g Arg	g Se:	r Sei 40	r Asn	Thi	r Va	l Va	1 G1 45	n I]	le T	hr	Cys		
Ar	g Ly 50		s Gl	u Lei	ı His	s Pr		u Phe	Hi:	s Gl	u As 60	sp Al	a Ly	ys V	al	Tyr		
Су · 65		n Gl	y Gl	u Le	u Va 70	l Me	t Th	r Thi	Gl:	y Gl 75	y Th	ır Ly	ys L	ys G	lu	Tyr 80		
Va	l Va	ıl As	p Va	1 Tr 85		r Gl	y As	n His	s Pr 90	o Pl	ne Ty	yr L	eu G	ly A	sn 95	Arg		
Se	r Al	la Le	eu M∈ 10		l As	p Al	a As	sp Gl:	n Va 5	1 G	lu L	ys P	he A	rg I	уs	Arg		

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Ile Ile Met Pro Thr Lys Lys Ser Lys Gly Pro Lys Gly Lys Lys Lys 130 135 140

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agg o	cat His	gtg Val	cag Gln 20	gcc Ala	aaa Lys	gaa Glu	tac Tyr	agg Arg 25	gaa Glu	cca Pro	aga Arg	gly aaa	tgt Cys 30	gtg Val	atg Met	96
aag a	Met	agc Ser 35	agt Ser	tta Leu	aaa Lys	gca Ala	cct Pro 40	gtt Val	ctg Leu	aga Arg	att Ile	cag Gln 45	gcc Ala	aca Thr	gaa Glu	144
tac a Tyr 1	aga Arg 50	gaa Glu	cca Pro	aga Arg	61Å 888	cgt Arg 55	gtg Val	aag Lys	atg Met	atg Met	tcc Ser 60	agt Ser	tta Leu	caa Gln	gca Ala	192
cct ( Pro ) 65	ctt Leu	ctg Leu	aca Thr	att Ile	cag Gln 70	agc Ser	ttc Phe	tca Ser	gjå aaa	tta Leu 75	agg Arg	gcc Ala	ccc Pro	agt Ser	gca Ala 80	240
tta ( Leu	gat Asp	tat Tyr	ttg Leu	gga Gly 85	agg Arg	cct Pro	agt Ser	cca Pro	ggt Gly 90	ttc Phe	ctt Leu	gtt Val	aag Lys	tat Tyr 95	aaa Lys	288
ctt Leu	gca Ala	aaa Lys	tca Ser 100	tct Ser	gly aaa	aga Arg	gaa Glu	aaa Lys 105	gct Ala	agc Ser	cga Arg	tgt Cys	gta Val 110	Pro	aaa Lys	336
gca Ala	atg Met	ttt Phe 115	gag Glu	cgt Arg	ttt Phe	acc Thr	gag Glu 120	Lys	gca Ala	att Ile	aag Lys	gto Val 125	Ile	atg Met	ctg Leu	384

tct Ser	caa Gln 130	gag Glu	gaa Glu	gct Ala	cgg Arg	aga Arg 135	ctt Leu	ggc Gly	cat His	Asn	ttt Phe 140	gtt Val	gly ggg	act Thr	ga Gl	g u	432
caa Gln 145	ata Ile	ctg Leu	ttg Leu	ggt Gly	cta Leu 150	att Ile	gga Gly	gaa Glu	Gly 999	act Thr 155	gjå aaa	att Ile	gcc Ala	gcc Ala	аа Ьу 16	S	480
gtt Val	ctt Leu	aaa Lys	tcc Ser	atg Met 165	gly aaa	atc Ile	aat Asn	ctt Leu	aaa Lys 170	gat Asp	tca Ser	cgc Arg	gtg Val	gaa Glu 175	. ۷ c	a al	<b>528</b>
gaa Glu	aag Lys	ata Ile	att Ile 180	ggg Gly	aga Arg	ggc	agt Ser	gga Gly 185	ttc Phe	gtg Val	gca Ala	gtg Val	gag Glu 190	att	. co	ca ro	576
ttt Phe	act Thr	cct Pro 195	Arg	gca Ala	aag Lys	cgg Arg	gtg Val 200	ctg Leu	gag Glu	ttg Leu	tca Ser	cta Leu 205	Gru	.gaa Glu	age aA	ct la	624
cga Arg	caa Gln 210	Leu	ggg	cat His	aac Asn	tac Tyr 215	att Ile	ggt Gly	tca Ser	gag Glu	cac His	Leu	ttg Leu	ctt Le:	g g G	gt ly	672
cta Leu 225	Leu	cgt Arg	gaa Glu	ggg	gag Glu 230	ggt Gly	gtg Val	gca Ala	gct Ala	cgt Arg 235	val	ttg L Lei	g gag ı Glu	aai As:		tg eu 40	720
ggt Gly	gca Ala	gat Asp	cct Pro	agt Ser 245	aat Asn	ata Ile	cgg	aca Thr	cag Gln 250	Val	ata Ile	a cgt	ato g Met	gt Va 25	т С	ija iaa	768
gaa Glu	aac Asn	: aat 1 Asr	gaa Glu 260	ı Val	aca Thr	gca Ala	ago Ser	gtt Val 265	GT3	. GJŽ	g gga	a age y Se:	c ago c Sei 270	GI	a a y P	ac Asn	816
ago Sei	aaa Lys	a atg s Met 275	Pro	a aca o Thr	ctt Leu	gaa Glu	gag Gli 280	tyn	. GJ ² : 333	g act	c aa c As:	c tt n Le 28	u Tn	t aa r Ly	a o	cta Leu	864
gca Ala	a gag a Glu 290	ı Glı	g ggt u Gly	t aaa y Lys	a ct <u>c</u> s Lev	gat Asp 295	Pro	g gti o Vai	t gti l Val	t gga	a ag y Ar 30	g GI	g cc n Pr	a ca o Gl	ig a	atc Ile	912
gaa Gli 30	u Ar	a at	g gte t Va	c caq l Glı	g ato n Ile 310	e Let	ı Al	t cg	a ag	a ac g Th 31	т Гу	g aa 's As	ic aa sn As	c co n Pi	.0	tgt Cys 320	960
· ct Le	t at u Il	t gg e Gl	a ga y Gl	a cci u Pro 32	t gga o Gly s	a gti y Vai	t gg l Gl	t aa y Ly	g ac s Th 33	r Al	a at a Il	a go le Al	a ga la Gl	u G	ga ly 35	ctt Leu	1008
gc Al	a ca a Gl	g cg n Ar	a at g Il 34	e Al	t agi a Se:	t gg r Gl	t ga y As	t gt p Va 34	l Pr	t ga o Gl	a ac .u Th	ca at nr I	c ga le G] 35	.u G	gg ly	aag Lys	1056
ac Th	g gt r Va	t at 1 Il 35	e Th	c ct r Le	t ga u As	t at p Me	g gg t Gl 36	у Ге	t ct a Le	a gt eu Va	g go	la G	ga ao ly Tl 65	g a r L	aa ys	tac Tyr	1104

cgt Arg	gga Gly 370	gag Glu	ttc Phe	gag Glu	Glu	aga Arg 375	ttg Leu	aag Lys	aag Lys	ctt Leu	atg Met 380	gag Glu	gaa Glu	atc Ile	agg Arg	1152
caa Gln 385	agt Ser	gat Asp	gag Glu	ata Ile	att Ile 390	ctg Leu	ttt Phe	att Ile	gat Asp	gaa Glu 395	gtg Val	cac His	acg Thr	ctc Leu	atc Ile 400	1200
ggt Gly	gca Ala	gga Gly	gcc Ala	gct Ala 405	gaa Glu	ggt Gly	gcg Ala	atc Ile	gat Asp 410	gct Ala	gct Ala	aac Asn	atc Ile	tta Leu 415	aag Lys	1248
cca Pro	gct Ala	cta Leu	gca Ala 420	aga Arg	ggt Gly	gaa Glu	ttg Leu	cag Gln 425	tgt Cys	att Ile	ggt Gly	gca Ala	aca Thr 430	aca Thr	att Ile	1296
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gct Ala	ggg ggg	tct Ser 515	Arg	gtt Val	cga Arg	cta Leu	cgc Arg 520	His	gct Ala	cag Glr	g cti 1 Lei	cct Pro 52!	o Gli	g gaa u Gl	a gct u Ala	1584
aga Arg	gag Glu 530	Lev	gaa Glu	aag Lys	caa Glm	ctc Leu 535	Arg	g Cas	ato 11e	e acc	c aas r Ly: 54	s Gl	g aag u Ly	g aa s As	t gaa n Glu	1632
gct Ala 545	val	g cga	a ago g Ser	caa Glr	gac Asp 550	Phe	gag Glu	g ato 1 Met	g gct : Ala	gg a Gl; 55:	y Se	t ca r Hi	t cg s Ar	t ga g As	c cgt p Arg 560	1680
gaa Glu	ata 1 Ile	a gag e Glu	g cto 1 Leu	aag Lys 565	a Ala	gag Glu	g ata 1 Ile	a gct e Ala	a Asi	n Va	t tt l Le	a tc u Se	t cg r Ar	a gg g Gl 57	c aaa y Lys '5	1728
gaa Gli	a gto ı Val	g gco l Ala	c aaa a Lys 580	s Ala	e gag a Glu	g aat 1 Asi	gaa n Gl	a gci u Ala 58	a Gl	g ga u Gl	a gg u Gl	ga gg .y Gl	y Pr 59	o Tr	t gtc r Val	1776
aca Th:	a gaa r Gli	a tci u Sei 59:	r As	c ato o Ile	c caa e Gli	a cad	ate s Ile 60	e Va	c gc l Al	c ac a Th	c to r Tr	g ac p Th	ir Gi	ga at Ly II	c ccg Le Pro	1824

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cgt Arg	cct Pro	atc Ile	gcc Ala 660	agt Ser	ttc Phe	atc Ile	ttc Phe	tct Ser 665	ggt Gly	cca Pro	act Thr	Gly	gtt Val 670	gjà aaa	aaa Lys	2016
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gat As <u>r</u>	tto Phe 770	Lys	aac Asn	acg Thr	ctt Leu	ctg Leu 775	Ile	atg Met	act Thr	tca Ser	aac Asr 780	ı Val	Gly ggg	g ago 7 Sei	e agc	2352
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gaq Gli	g aaa 1 Lys	a gad s Asp	ago Ser	agt Ser 805	Туг	aac Asr	aga Arg	a ato g Ile	aag E Lys 810	s Ser	tta Lei	a gtç u Val	g act	r Gl	g gaa u Glu 5	2448
ct: Le	a aaa u Lys	a cag s Gli	g tat n Tyr 820	Phe	aga Arg	cca g Pro	gag Gli	g tto 1 Phe 82!	e Lei	g aad 1 Asi	c ag	g tt: g Le	a gat u Asj 83	p Gl	g atg u Met	2496
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Tyr Arg Glu Pro Arg Gly Arg Val Lys Met Met Ser Ser Leu Gln Ala 50 55 60

Pro Leu Leu Thr Ile Gln Ser Phe Ser Gly Leu Arg Ala Pro Ser Ala 65 70 75 80

Leu Asp Tyr Leu Gly Arg Pro Ser Pro Gly Phe Leu Val Lys Tyr Lys 85 90 95

- Leu Ala Lys Ser Ser Gly Arg Glu Lys Ala Ser Arg Cys Val Pro Lys
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- Ala Met Phe Glu Arg Phe Thr Glu Lys Ala Ile Lys Val Ile Met Leu 115 120 125
- Ser Gln Glu Glu Ala Arg Arg Leu Gly His Asn Phe Val Gly Thr Glu 130 135 140
- Gln Ile Leu Leu Gly Leu Ile Gly Glu Gly Thr Gly Ile Ala Ala Lys 145 150 155 160
- Val Leu Lys Ser Met Gly Ile Asn Leu Lys Asp Ser Arg Val Glu Val 165 170 175
- Glu Lys Ile Ile Gly Arg Gly Ser Gly Phe Val Ala Val Glu Ile Pro 180 185 190
- Phe Thr Pro Arg Ala Lys Arg Val Leu Glu Leu Ser Leu Glu Glu Ala 195 200 205
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- Glu Asn Asn Glu Val Thr Ala Ser Val Gly Gly Gly Ser Ser Gly Asn 260 265 270
- Ser Lys Met Pro Thr Leu Glu Glu Tyr Gly Thr Asn Leu Thr Lys Leu 275 280 285
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Ala Gln Arg Ile Ala Ser Gly Asp Val Pro Glu Thr Ile Glu Gly Lys 340 345 350

Thr Val Ile Thr Leu Asp Met Gly Leu Leu Val Ala Gly Thr Lys Tyr 355 360 365

Arg Gly Glu Phe Glu Glu Arg Leu Lys Lys Leu Met Glu Glu Ile Arg 370 375 380

Gln Ser Asp Glu Ile Ile Leu Phe Ile Asp Glu Val His Thr Leu Ile 385 390 395 400

Gly Ala Gly Ala Glu Gly Ala Ile Asp Ala Ala Asn Ile Leu Lys 405 410 415

Pro Ala Leu Ala Arg Gly Glu Leu Gln Cys Ile Gly Ala Thr Thr Ile 420 425 430

Asp Glu Tyr Arg Lys His Ile Glu Lys Asp Pro Ala Leu Glu Arg Arg 435 440 445

Phe Gln Pro Val Lys Val Pro Glu Pro Thr Val Glu Glu Ala Ile Gln 450 455 460

Ile Leu Gln Gly Leu Arg Glu Arg Tyr Glu Ile His His Lys Leu Arg 465 470 475 480

Tyr Thr Asp Glu Ala Leu Val Ala Ala Ala Gln Leu Ser His Gln Tyr 485 490 495

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Glu Ile Glu Leu Lys Ala Glu Ile Ala Asn Val Leu Ser Arg Gly Lys 565 570 575

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- Thr Glu Ser Asp Ile Gln His Ile Val Ala Thr Trp Thr Gly Ile Pro 595 600 605
- Val Glu Lys Val Ser Ser Asp Glu Ser Ser Arg Leu Leu Gln Met Glu 610 620
- Gln Thr Leu His Thr Arg Val Ile Gly Gln Asp Glu Ala Val Lys Ala 625 630 635 640
- Ile Ser Arg Ala Ile Arg Arg Ala Arg Val Gly Leu Lys Asn Pro Asn 645 650 655
- Arg Pro Ile Ala Ser Phe Ile Phe Ser Gly Pro Thr Gly Val Gly Lys 660 665 670
- Ser Glu Leu Ala Lys Ala Leu Ala Ala Tyr Tyr Phe Gly Ser Glu Glu 675 680 685
- Ala Met Ile Arg Leu Asp Met Ser Glu Phe Met Glu Arg His Thr Val 690 695 700
- Ser Lys Leu Ile Gly Ser Pro Pro Gly Tyr Val Gly Tyr Thr Glu Gly 705 710 715 720
- Gly Gln Leu Thr Glu Ala Val Arg Arg Pro Tyr Thr Leu Val Leu 725 730 735
- Phe Asp Glu Ile Glu Lys Ala His Pro Asp Val Phe Asn Met Met Leu 740 745 750
- Gln Ile Leu Glu Asp Gly Arg Leu Thr Asp Ser Lys Gly Arg Thr Val 755 760 765
- Asp Phe Lys Asn Thr Leu Leu Ile Met Thr Ser Asn Val Gly Ser Ser 770 775 780
- Val Ile Glu Lys Gly Gly Arg Arg Ile Gly Phe Asp Leu Asp His Asp 785 790 795 800

Glu Lys Asp Ser Ser Tyr Asn Arg Ile Lys Ser Leu Val Thr Glu Glu 805 810 815

Leu Lys Gln Tyr Phe Arg Pro Glu Phe Leu Asn Arg Leu Asp Glu Met 820 825 830

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Ile Met Leu Lys Glu Val Val Ala Arg Leu Glu Val Lys Glu Ile Glu 850 860

Leu Gln Val Thr Glu Arg Phe Lys Glu Arg Val Val Asp Glu Gly Phe 865 870 875 880

Asp Pro Ser Tyr Gly Ala Arg Pro Leu Arg Arg Ala Ile Met Arg Leu 885 890 895

Leu Glu Asp Ser Met Ala Glu Lys Met Leu Ser Arg Asp Ile Lys Glu 900 905 910

Gly Asp Ser Val Ile Val Asp Val Asp Ala Glu Gly Ser Val Val Val 915 920 925

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ct Le	g at u Il 13	e As	t cag p Gli	g aag n Lys	g aag E Lys	tac Tyr 135	: Ası	gag n Glu	g gct 1 Ala	aaa A Lys	a gct s Ala 14	а Су	t tc s Se	t tc r Se	a gca r Ala	432
a9 Se 14	er Il	t gc e Al	t cgi a Arg	t cto	2 aag 1 Lys 150	s Ası	gte n Va	c aad l Ası	c cga	a agg g Arg 15	g Th	c at r Il	t ga e As	t gt p Va	g ata l Ile 160	:
gc Al	a to la Se	a ag r Ar	a cto	c tac u Ty: 16!	r Phe	t tac	c ta r Ty	t tci r Se:	t ttg r Lei 17	u Se	t ta r Ty	t ga r Gl	ıg ca .u Gl	a ac n Th	c ggt r Gly '5	528
ga As	at ct sp Le	t go eu Al	t ga a Gl 18	u Il	t cg	g Gl	t ac y Th	t ct r Le 18	u Le	t gc u Al	g tt a Le	g ca u Hi	at ca is Hi 19	s se	et gca er Ala	a 576 a
a T	eg et hr Le	a ag eu Ar 19	g Hi	c ga s As	t ga p Gl	g ct u Le	g gg u Gl 20	y Gl	g ga n Gl	a ac u Th	c ct r Le	eu Le	eu As 05	ac ci sn Le	eu Le	g 624 u
F.	eu A	gt aa rg As 10	ac ta sn Ty	t tt T Le	g ca u Hi	t ta s Ty 21	r As	c ct n Le	c ta u Ty	it ga r As	it ca sp GI 22	Ln A.	ca ga la G	ag a lu L	ag ct ys Le	a 672 u
a	ga t	ca aa	ag go	a co	t cg	c tt	t ga	g go	et ca	it to	ca a	ac c	aa c	ag t	tt tg	t 720

Arg 225	Ser	Lys	Ala	Pro	Arg 230	Phe (	Glu i	Ala :	His S	Ser <i>l</i> 235	Asn (	Gln (	Gln	Phe	Cy:	s 0	
agg Arg	tac Tyr	ctt Leu	ttc Phe	tat Tyr 245	ctc Leu	GJÀ aaa	aag Lys	Ile	cgt a Arg ' 250	act a	att Ile	cag Gln	ctc Leu	gaa Glu 255	ta Ty	t r	768
acg Thr	gac Asp	gca Ala	aaa Lys 260	gag Glu	agc Ser	ctt Leu	ctt Leu	cag Gln 265	gcg Ala	gcc Ala	agg Arg	aaa Lys	gcc Ala 270	cct Pro	at Il	a .e	816
gca Ala	gct Ala	ttg Leu 275	ggc Gly	ttc Phe	agg Arg	atc Ile	caa Gln 280	tgc Cys	aat Asn	aaa Lys	tgg Trp	gca Ala 285	att Ile	ctg Leu	gt Va	t al	864
cgt Arg	cta Leu 290	Leu	ctg Leu	ggt Gly	gag Glu	ata Ile 295	cca Pro	gag Glu	cgt Arg	tct Ser	atc Ile 300	ttc Phe	act Thr	caa Gln	ı aa ı Ly	ag Ys	912
ggt Gly 305	Met	gag Glu	aag Lys	gcc Ala	ctc Leu 310	aga Arg	ccc Pro	tac Tyr	ttc Phe	gag Glu 315	cta Leu	aca Thr	aat Asn	gcc Ala	a V	tt al 20	960
agg Arg	att Ile	. Gly	gac Asp	ttg Leu 325	Glu	ttg Leu	ttt Phe	agg Arg	aca Thr 330	gtc Val	cag Gln	gag Glu	aag Lys	tto Pho	e T	tg eu	1008
gac Asr	aca Thi	ttt Phe	gct Ala 340	Glr	gac Asp	aga Arg	acg Thr	cac His	aat Asn	ctc Leu	atc Ile	gtg Val	cga Arg 350	J пе	c c u A	gc rg	<b>1056</b>
cac His	aat Asi	z gto n Val	l Ile	agg Arg	g act g Thr	gga Gly	ctg Leu 360	Arg	j aac j Asn	ata Ile	agt Ser	ato Ile	5 Se	c ta r Ty	c t	ca Ser	1104
aga Arg	a ato	e Se	t tta r Le	a cco	c gat o As <u>r</u>	gtt Val	. Ala	aaa Lys	a aag s Lys	ctg Leu	agg Arg 380	д тел	c aa ı As:	c to n Se	t c	gaa 3lu	1152
aa As: 38	n Pr	t gt o Va	g gc	t ga ^r a As _l	t gcg p Ala 39	a Glu	ago 1 Sei	ato	c gto e Val	g gca Ala 395	т г.	g gco s Ala	c at a Il	a co e Ar	.g 4	gac Asp 400	1200
g1 aa	a gc y Al	t at a Il	t ga e As	t gc p Al 40	a Th	a ato r Ile	c gat e Asj	t cae	c aaa s Ly: 410	s Ası	gg n Gl	a tg y Cy	c at s Me	C V	al 15	tcc Ser	1248
aa Ly	a ga s Gl	a ac u Th	t gg r Gl 42	y As	c at p Il	c tac e Ty:	c to r Se:	g ac r Th 42	g aat r Asi 5	t gag n Gli	g cc u Pr	a ca o Gl	a ac n Th 43	ir A	cg la	ttc Phe	1296
aa As	ic to in Se	a ag er Ar 43	g Il	t go e Al	t tt a Ph	c tg e Cy	c ct s Le 44	u As	c at	g ca t Hi	t aa s As	c ga n Gl 44	u A	et g la V	tc al	aga Arg	1344
g( A)	la Le	eu Ar	gg tt g Ph	t co ne Pr	et co o Pr	t aa o As 45	n Th	t ca r Hi	ıc aa .s Ly	g ga s Gl	g aa u Ly 46	s GJ	aa ag lu Se	gc g er A	at sp	gag Glu	1392
aa	ag a	gg ag	ga ga	ag ag	gg aa	ıg ca	a ca	ig ga	aa ga	a ga	ıg ct	t go	ct a	ag c	at	atg	1440

Lys Arg Arg Glu Arg Lys Gln Gln Glu Glu Glu Leu Ala Lys His Met 465 470 475 480

gct gag gaa gac gat gat gat ttt tag Ala Glu Glu Asp Asp Asp Phe 485 1467

<210> 84

<211> 488

<212> PRT

<213> Arabidopsis thaliana

<400> 84

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Ile Ile Ser Ser Ser Thr Ser Thr Met Gln Asn Leu Lys Glu Ile Ala 20 25 30

Ala Leu Ile Asp Thr Gly Ser Tyr Thr Lys Glu Val Arg Arg Ile Ala 35 40 45

Arg Ala Val Arg Leu Thr Ile Gly Leu Arg Gln Lys Leu Thr Gly Ser 50 60

Val Leu Ser Ser Phe Leu Asp Phe Ala Leu Val Pro Gly Ser Glu Ala 65 70 75 80

His Ser Arg Leu Ser Ser Phe Val Pro Lys Gly Asp Glu His Asp Met 85 90 95

Glu Val Asp Thr Ala Ser Ser Ala Thr Gln Ala Ala Pro Ser Lys His 100 105 110

Leu Pro Ala Glu Leu Glu Ile Tyr Cys Tyr Phe Ile Val Leu Leu Phe 115 120 125

Leu Ile Asp Gln Lys Lys Tyr Asn Glu Ala Lys Ala Cys Ser Ser Ala 130 135 140

Ser Ile Ala Arg Leu Lys Asn Val Asn Arg Arg Thr Ile Asp Val Ile 145 150 155 160 Ala Ser Arg Leu Tyr Phe Tyr Tyr Ser Leu Ser Tyr Glu Gln Thr Gly 165 170 175

- Asp Leu Ala Glu Ile Arg Gly Thr Leu Leu Ala Leu His His Ser Ala 180 185 190
- Thr Leu Arg His Asp Glu Leu Gly Gln Glu Thr Leu Leu Asn Leu Leu 195 200 205
- Leu Arg Asn Tyr Leu His Tyr Asn Leu Tyr Asp Gln Ala Glu Lys Leu 210 215 220
- Arg Ser Lys Ala Pro Arg Phe Glu Ala His Ser Asn Gln Gln Phe Cys 225 230 235 240
- Arg Tyr Leu Phe Tyr Leu Gly Lys Ile Arg Thr Ile Gln Leu Glu Tyr 245 250 255
- Thr Asp Ala Lys Glu Ser Leu Leu Gln Ala Ala Arg Lys Ala Pro Ile 260 265 270
- Ala Ala Leu Gly Phe Arg Ile Gln Cys Asn Lys Trp Ala Ile Leu Val 275 280 285
- Arg Leu Leu Gly Glu Ile Pro Glu Arg Ser Ile Phe Thr Gln Lys 290 295 300
- Gly Met Glu Lys Ala Leu Arg Pro Tyr Phe Glu Leu Thr Asn Ala Val 305 310 315 320
- Arg Ile Gly Asp Leu Glu Leu Phe Arg Thr Val Gln Glu Lys Phe Leu 325 330 335
- Asp Thr Phe Ala Gln Asp Arg Thr His Asn Leu Ile Val Arg Leu Arg 340 345 350
- His Asn Val Ile Arg Thr Gly Leu Arg Asn Ile Ser Ile Ser Tyr Ser 355 360 365
- Arg Ile Ser Leu Pro Asp Val Ala Lys Lys Leu Arg Leu Asn Ser Glu 370 375 380
- Asn Pro Val Ala Asp Ala Glu Ser Ile Val Ala Lys Ala Ile Arg Asp 385 390 395 400

Gly Ala Ile Asp Ala Thr Ile Asp His Lys Asn Gly Cys Met Val Ser Lys Glu Thr Gly Asp Ile Tyr Ser Thr Asn Glu Pro Gln Thr Ala Phe 425 420 Asn Ser Arg Ile Ala Phe Cys Leu Asn Met His Asn Glu Ala Val Arg 440 435 · Ala Leu Arg Phe Pro Pro Asn Thr His Lys Glu Lys Glu Ser Asp Glu 455 Lys Arg Arg Glu Arg Lys Gln Gln Glu Glu Leu Ala Lys His Met 475 470 465 Ala Glu Glu Asp Asp Asp Phe 485 <210> 85 <211> 282 DNA <212> <213> Arabidopsis thaliana <220> CDS <221> (1) . . (282) <222> <223> 68181 <400> 85 atg gac gca agc atg atg gct gga ctt gat ggt ctt cct gaa gaa gac 48 Met Asp Ala Ser Met Met Ala Gly Leu Asp Gly Leu Pro Glu Glu Asp aaa gcc aaa atg gcc tcc atg atc gat cag ctt cag ctc cgt gat agt 96 Lys Ala Lys Met Ala Ser Met Ile Asp Gln Leu Gln Leu Arg Asp Ser 25 20 ttg agg atg tac aat tca ttg gtg gag agg tgt ttc gtg gac tgt gtt 144 Leu Arg Met Tyr Asn Ser Leu Val Glu Arg Cys Phe Val Asp Cys Val 40 35 gat agc ttc aca cgc aaa tct ctg cag aaa caa gag gag act tgt gtg 192

Asp Ser Phe Thr Arg Lys Ser Leu Gln Lys Gln Glu Glu Thr Cys Val

50

atg cgt tgc gct gag aag ttc ctt aag cat acg atg cgt gtt ggt atg 240 Met Arg Cys Ala Glu Lys Phe Leu Lys His Thr Met Arg Val Gly Met 65 70 75 80

cgg ttt gct gag ctc aat cag aac gca cca acc caa gac tga 282 Arg Phe Ala Glu Leu Asn Gln Asn Ala Pro Thr Gln Asp 85 90

<210> 86

<211> 93

<212> PRT

<213> Arabidopsis thaliana

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Lys Ala Lys Met Ala Ser Met Ile Asp Gln Leu Gln Leu Arg Asp Ser 20 25 30

Leu Arg Met Tyr Asn Ser Leu Val Glu Arg Cys Phe Val Asp Cys Val 35 40 45

Asp Ser Phe Thr Arg Lys Ser Leu Gln Lys Gln Glu Glu Thr Cys Val 50 55 60

Met Arg Cys Ala Glu Lys Phe Leu Lys His Thr Met Arg Val Gly Met 65 70 75 80

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<210> 87

<211> 816

<212> DNA

<213> Arabidopsis thaliana

<220>

<221> CDS

<222> (1)..(816)

<223> 70913

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cat His	gct Ala	gtt Val	cag Gln 20	cag Gln	ccg Pro	atg Met	atg Met	tat Tyr 25	gca Ala	gag Glu	ccc Pro	tgg Trp	tgg Trp 30	aaa Lys	aac			96
aac Asn	tcc Ser	ttt Phe 35	ggt Gly	gtt Val	gta Val	cct Pro	caa Gln 40	gcg Ala	aga Arg	cct Pro	tct Ser	gga Gly 45	att Ile	cca Pro	tca Ser	1 :	:	.44
aat Asn	tcc Ser 50	tct Ser	tct Ser	ttg Leu	gat Asp	tgc Cys 55	ccc	aat Asn	ggt Gly	tcc Ser	gag Glu 60	tca Ser	aac Asn	gat Asp	gtt Val	į		L92
cat His 65	tca Ser	gca Ala	tct Ser	gaa Glu	gac Asp 70	ggt Gly	gcg Ala	ttg Leu	aat Asn	ggt Gly 75	gaa Glu	aac Asn	gat Asp	GJ ^y ggc	ac Th	_	. :	240
tgg Trp	aag Lys	gat Asp	tca Ser	caa Glr 85	gct Ala	gca Ala	act Thr	tcc Ser	tct Ser 90	cgt Arc	tca Sei	a gat Asp	aat Asr	cac His	gg Gl	a Y		288
atg Met	gaa Glu	ı gga	a aat 7 Asi 100	ı Ası	c cca	gcg Ala	g cto Lei	tct Ser 105	: TTE	e cgt	aad J Asi	ato n Met	g cat His	o FLO	t ca p Gl	g .n	•	336
cca	a cti	gt: 1 Va:	l Gl	a cca	a cca o Pro	a gag o Gli	g cti Lei 12	ı va.	gga l Gl	a cad	c ta s Ty:	t ator Ilo	C AI	t tg a Cy	t gt s Va	c il		384
Pro	a aa o As: 13	n Pr	a ta o Ty	t ca r Gl	g gat n Asj	p Pro	э Ту	t tai	t ggg r Gl	y Gl	a tt y Le 14	u Me	g gg t Gl	a gc y Al	a ta .a Ty	at yr		432
99 ¹ Gl	у Ні	t ca s Gl	g ca n Gl	a tt n Le	g gg u Gl 15	y Ph	t cg e Ar	t cc g Pr	a ta o Ty	t ct r Le 15	u Gi	a at y Me	g cc t Pr	t cg o Ar	. 5	aa lu 60		480
ag Ar	a ac g Th	a go r Al	t ct a Le	g cc u Pr 16	a ct o Le	t ga u As	c at p Me	g go t Al	a ca a Gl 17	и сл	g co u Pi	c gt	t ta l Ty		g a al A 75	at sn		528
gc Al	a aa a Ly	ıg ca rs Gl	ig ta .n Ty 18	r G]	ig gg Lu Gl	a at y Il	t ct e Le	a ag eu Ar 18	gAr	ga ag gg Ai	ga aa	aa go ys Al	ca co La Ai 19	.y A	cc a la I	ys iys		576
gc Al	a ga la Gl	lu Le	a ga eu Gl 95	ig ag Lu Ai	gg aa rg Ly	ia gt vs Va	al I.	cc cg le Ai	g As	ac ag sp Ai	ga a rg L	ys P.	ca ta ro T 05	at c yr L	tt o eu F	ac Iis į		624
ga	ag to	ca ag	ga ca	ac a	ag ca	at go	ca a	tg a	ga ag	gg g	ca c	ga g	cg ·a	gt g	ga g	ggc		672

Glu	Ser 210	Arg	His	Lys	His	Ala 215	Met	Arg	Arg	Ala	Arg 220	Ala	Ser	Gly	Gly	
										gga Gly 235						720
										tca Ser						768
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<210> 88

<211> 271

<212> PRT

<213> Arabidopsis thaliana

<400> 88

Met Gln Ser Lys Pro Gly Arg Glu Asn Glu Glu Glu Val Asn Asn His 1 5 10 15

His Ala Val Gln Gln Pro Met Met Tyr Ala Glu Pro Trp Trp Lys Asn 20 25 30

Asn Ser Phe Gly Val Val Pro Gln Ala Arg Pro Ser Gly Ile Pro Ser 35 40 45

Asn Ser Ser Ser Leu Asp Cys Pro Asn Gly Ser Glu Ser Asn Asp Val 50 55 60

His Ser Ala Ser Glu Asp Gly Ala Leu Asn Gly Glu Asn Asp Gly Thr 65 70 75 80

Trp Lys Asp Ser Gln Ala Ala Thr Ser Ser Arg Ser Asp Asn His Gly 85 90 95

Met Glu Gly Asn Asp Pro Ala Leu Ser Ile Arg Asn Met His Asp Gln 100 105 110

Pro Leu Val Gln Pro Pro Glu Leu Val Gly His Tyr Ile Ala Cys Val 115 120 125

Pro Asn Pro Tyr Gln Asp Pro Tyr Tyr Gly Gly Leu Met Gly Ala Tyr 130 135 140

Gly His Gln Gln Leu Gly Phe Arg Pro Tyr Leu Gly Met Pro Arg Glu 145 150 155 160

Arg Thr Ala Leu Pro Leu Asp Met Ala Gln Glu Pro Val Tyr Val Asn 165 170 175

Ala Lys Gln Tyr Glu Gly Ile Leu Arg Arg Arg Lys Ala Arg Ala Lys 180 185 190

Ala Glu Leu Glu Arg Lys Val Ile Arg Asp Arg Lys Pro Tyr Leu His 195 200 205

Glu Ser Arg His Lys His Ala Met Arg Arg Ala Arg Ala Ser Gly Gly
210 215 220

Arg Phe Ala Lys Lys Ser Glu Val Glu Ala Gly Glu Asp Ala Gly Gly 225 230 235

Arg Asp Arg Glu Arg Gly Ser Ala Thr Asn Ser Ser Gly Ser Glu Gln 245 250 255

Val Glu Thr Asp Ser Asn Glu Thr Leu Asn Ser Ser Gly Ala Pro 260 265 270

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<220>

<221> CDS

<222> (1)..(990)

<223> 71067

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1 5 10 15

48

tct Ser	gac Asp	ggt Gly	ttt Phe 20	gat Asp	tat Tyr	ccc Pro	gac Asp	ggt Gly 25	atc Ile	cca Pro	ata Ile	tca Ser	tac Tyr 30	aat Asi	ı C	tt eu	96	
cat His	agg Arg	ctt Leu 35	cgt Arg	cac His	ttt Phe	gag Glu	tgt Cys 40	gaa Glu	ggc Gly	agt Ser	tat Tyr	Pro 45	aag Lys	ta Ty	t c	ro	144	
tat Tyr	ggt Gly 50	tct Ser	ttg Leu	gtc Val	áag Lys	ttt Phe 55	tat Tyr	gca Ala	atg Met	gtg Val	gga Gly 60	ctt Leu	cat His	cg Ar	t t	ac Tyr	192	
aat Asn 65	gtg Val	ttg Leu	gag Glu	Gly aaa	aaa Lys 70	aat Asn	ttg Leu	cag Gln	ctc Leu	gat Asp 75	acc Thr	c cta	a aag 1 Lys	g ag s Se		tc Phe 80	240	
aac Asn	atg Met	aga Arg	atc   Ile	aat Asn 85	tgt Cys	ggt Gly	gct Ala	tct Ser	tct Ser 90	tac Tyr	tac Ty	c at	t act	t tt r Le 9!	-u -	gct Ala	288	
gca Ala	cgc	gtt Val	cca Pro	) Asp	agc Ser	ggt	ttg Leu	aag Lys 105	GII	ato Ile	tt Ph	t ca e Gl	g gt n Va 11		ta eu	gtt Val	336	
cat His	gaa Glu	gag Glu	g egt 1 Arg	ctt J Lev	ggc Gly	agt Ser	tta Leu 120	ı Asp	ato Met	g aca	a tg r Cy	t ac s Th	T TI	cg eA	ct la	aga Arg	384	
cct Pro	cga Arg	y Vai	g act	aco r Thi	aat Asr	gtg Val	L Pro	ttt D Phe	cta e Lei	a cg ı Ar	t cc g Pr 14	O A	ic ag is Se	c g	aa lu	tca Ser	432	
gag Glu 14!	ı Ty	ga r As	t ta p Ty:	t ato	g gad t Asp 150	o Asi	t ga ^r n Asj	t gaa p Gli	a tt u Le	g cc u Pr 15	O AS	ac to	gg co	et t	ca Ser	gag Glu 160	480	
at: Il	t gc e Al	t tt a Ph	c ga e As	t ga p As 16	p Th	a aa r Ly	a cg s Ar	g tt g Ph	t ca e Hi 17	s re	g gt	tg a	ag ga	Lu s	ca Ser 175	gag Glu	528	
tt Le	g cg u Ar	a ga g As	c aa p As 18	n As	t tg p Tr	g at p Il	t cg e Ar	a ct g Le 18	и Ту	t tt r Le	g g eu G	aa c lu L	eu 1	ca e hr 1 90	ctt Leu	gtt Val	576	
gc Al	t ca a Hi	c ga s As	p Ar	g tt g Ph	t ct e Le	t ac	a gt ir Va 20	IT HI	c ta s Ty	t ci	tc t eu S	er e	ag t ln L	tg eu	gag Glu	att Ile	624	:
gt Va	g as	rs Va	t go	g at la Il	t ga .e Gl	a ga u Gl 21	u va	g ga al Gl	ig ca lu Gi	aa c	TO H	at g sn <i>I</i> 20	gcg a	gt Ser	cto	aac Asn	672	<b>!</b>
ac Th	ır Ly	aa ao /s Tì	et ac	ca tt nr Ph	t gt ne Va 23	al Ty	ac at /r I:	ta ad le Tì	et to	уr ь	ag g ys <i>I</i> 35	ac t	ttg g Leu <i>l</i>	jca Nla	aag Lys	g gct s Ala 240		)
G:	ag a	tt g le G	gt ga ly G	lu P	cg gt ro Va 45	al A	at c	gc a rg L	ys A	ct a la I 50	tt q	gtt ( Val )	aga a Arg 1	aaa Lys	ate 116 25	c ato e Ile 5	761	8

aat Asn	gag Glu	act Thr	acg Thr 260	gga Gly	ctc Leu	ttg Leu	aga Arg	ctc Leu 265	cgg Arg	ggt Gly	gat Asp	tat Tyr	tgg Trp 270	agt Ser	gga Gly	816
gaa Glu	aga Arg	agt Ser 275	gtg Val	atc Ile	act Thr	ccg Pro	gag Glu 280	gag Glu	gaa Glu	tat Tyr	atg Met	ctt Leu 285	ctc Leu	cat His	ggc	864
gga Gly	gaa Glu 290	aaa Lys	gtt Val	cga Arg	aac Asn	aat Asn 295	gag Glu	cag Gln	cgt Arg	Ser	aaa Lys 300	aaa Lys	ctt Leu	aag Lys	cgt Arg	<b>912</b>
cgt Arg 305	Val	ggt Gly	gtt Val	cat His	agg Arg 310	cta Leu	tgg Trp	cga Arg	tgg Trp	tgg Trp 315	Tyr	Cag Gln	gct Ala	tac Tyr	aaa Lys 320	960
				cgc Arg 325	Ser								-			990

<210> 90

<211> 329

<212> PRT

<213> Arabidopsis thaliana

<400> 90

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Ser Asp Gly Phe Asp Tyr Pro Asp Gly Ile Pro Ile Ser Tyr Asn Leu 20 25 30

His Arg Leu Arg His Phe Glu Cys Glu Gly Ser Tyr Pro Lys Tyr Pro 35 40 45

Tyr Gly Ser Leu Val Lys Phe Tyr Ala Met Val Gly Leu His Arg Tyr 50 55 60

Asn Val Leu Glu Gly Lys Asn Leu Gln Leu Asp Thr Leu Lys Ser Phe 65 70 75 80

Asn Met Arg Ile Asn Cys Gly Ala Ser Ser Tyr Tyr Ile Thr Leu Ala 85 90 95

Ala Arg Val Pro Asp Ser Gly Leu Lys Gln Ile Phe Gln Val Leu Val 100 105 110

His Glu Glu Arg Leu Gly Ser Leu Asp Met Thr Cys Thr Ile Ala Arg 115 120 125

Pro Arg Val Thr Thr Asn Val Pro Phe Leu Arg Pro His Ser Glu Ser 130

Glu Tyr Asp Tyr Met Asp Asn Asp Glu Leu Pro Asp Trp Pro Ser Glu 145 150 155 160

Ile Ala Phe Asp Asp Thr Lys Arg Phe His Leu Val Lys Glu Ser Glu 165 170 175

Leu Arg Asp Asn Asp Trp Ile Arg Leu Tyr Leu Glu Leu Thr Leu Val

Ala His Asp Arg Phe Leu Thr Val His Tyr Leu Ser Gln Leu Glu Ile 195 200 205

Val Lys Val Ala Ile Glu Glu Val Glu Gln Pro Asn Ala Ser Leu Asn 210 215 220

Thr Lys Thr Thr Phe Val Tyr Ile Thr Tyr Lys Asp Leu Ala Lys Ala 225 230 235 240

Gln Ile Gly Glu Pro Val Asp Arg Lys Ala Ile Val Arg Lys Ile Ile 245 250 255

Asn Glu Thr Thr Gly Leu Leu Arg Leu Arg Gly Asp Tyr Trp Ser Gly 260 265 270

Glu Arg Ser Val Ile Thr Pro Glu Glu Glu Tyr Met Leu Leu His Gly 275 280 285

Gly Glu Lys Val Arg Asn Asn Glu Gln Arg Ser Lys Lys Leu Lys Arg 290 295 300

Arg Val Gly Val His Arg Leu Trp Arg Trp Trp Tyr Gln Ala Tyr Lys 305 310 315

Asn Arg Gly Leu Arg Ser Ser Ser Tyr 325

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<222> (1)..(1614)

<223> 71654

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tct Ser	tca Ser	agg Arg	ttt Phe 20	ggt Gly	tcg Ser	ctt Leu	tac Tyr	gtc Val 25	ggt Gly	gat Asp	ctt Leu	agc Ser	cca Pro 30	gac Asp	gtg Val	<u>9</u>	96
acg Thr	gag Glu	aaa Lys 35	gat Asp	ctc Leu	att Ile	gat Asp	aag Lys 40	ttc Phe	tct Ser	ttg Leu	aat Asn	gtt Val 45	ccg Pro	gta Val	gtg Val	14	14
tcc Ser	gtt Val 50	cat His	ctt Leu	tgc Cys	cgt Arg	aac Asn 55	tct Ser	gtc Val	acc Thr	gga Gly	aaa Lys 60	tcc Ser	atg Met	tgt Cys	tac Tyr	1:	92
gct Ala 65	tac Tyr	atc Ile	aac Asn	ttc Phe	gat Asp 70	tca Ser	cct Pro	ttc Phe	agc Ser	gca Ala 75	tcg Ser	aat Asn	gct	atg Met	act Thr 80	<b>2</b>	40
cgc Arg	tta Leu	aac Asn	cat His	agt Ser 85	gat Asp	ttg Leu	aag Lys	gga Gly	aag Lys 90	gct Ala	atg Met	cga Arg	ata Ile	atg Met 95	tgg Trp		88
tct Ser	. cag	agg Arg	gat Asp 100	Leu	gcg Ala	tac Tyr	cgt Arg	cgt Arg 105	Arg	act Thr	cgt Arg	act Thr	ggt Gly 110	Phe	gca Ala		36
aat Asn	cta Lev	tac Tyr 115	Val	aag Lys	aat Asn	ctg Leu	gat Asp 120	Ser	tcg Ser	att Ile	act Thr	ago Ser 125	Sei	tgc Cys	tta Leu	3	884
gag	cga Arg 130	g Met	ttt: Phe	tgo Cys	ccc Pro	ttt Phe 135	Gly	tco Ser	ata Ile	ctt Lev	tct Sei 140	c Cys	aaa Lys	a gto s Val	gtt Val	•	132
gaa Glu 149	ı Gl	g aat 1 Asr	gg gg	caa / Glr	agt Ser 150	Lys	ggt Gly	ttt / Phe	ggc Gly	Pho 15	e va.	t cag	g tti n Pho	t gai e Asj	t aca p Thr 160	•	480
gag	g ca	a tct	gct	gta	a tct	gct	cgt	tet	gct	cto	c ca	c gg	c tc	t at	g gtt		528

Glu Gln Ser Ala Val Ser Ala Arg Ser Ala Leu His Gly Ser Met Val 165 170 175	
tat ggc aag aaa ctg ttt gtt gcc aag ttc atc aac aag gat gaa aga Tyr Gly Lys Leu Phe Val Ala Lys Phe Ile Asn Lys Asp Glu Arg 180 185 190	576
gca gct atg gca gga aat caa gac tct aca aac gtt tat gtg aag aat Ala Ala Met Ala Gly Asn Gln Asp Ser Thr Asn Val Tyr Val Lys Asn 195 200 205	624
ctg atc gaa act gtt aca gat gat tgt cta cat aca ctg ttt tct caa Leu Ile Glu Thr Val Thr Asp Asp Cys Leu His Thr Leu Phe Ser Gln 210 215 220	672
tat gga act gtc tct agt gtt gtg gtt atg agg gat ggt atg gga aga Tyr Gly Thr Val Ser Ser Val Val Val Met Arg Asp Gly Met Gly Arg 235 240	720
tct aga ggt ttc gga ttt gtt aac ttc tgc aat cca gaa aat gct aag Ser Arg Gly Phe Gly Phe Val Asn Phe Cys Asn Pro Glu Asn Ala Lys 245 250 255	768
aaa gct atg gaa tct ctc tgt gga cta caa ctt gga tcg aag aaa ttg Lys Ala Met Glu Ser Leu Cys Gly Leu Gln Leu Gly Ser Lys Leu 260 265 270	816
ttt gtt ggt aag gca ctc aag aaa gat gaa agg agg gag atg ctg aaa Phe Val Gly Lys Ala Leu Lys Lys Asp Glu Arg Arg Glu Met Leu Lys 275 280 285	864
cag aaa ttc agt gac aac ttt att gca aag cct aac atg aga tgg tcc Gln Lys Phe Ser Asp Asn Phe Ile Ala Lys Pro Asn Met Arg Trp Ser 290 295 300	912
aat ctg tac gtg aag aac ttg agt gaa tca atg aat gaa aca aga ctg Asn Leu Tyr Val Lys Asn Leu Ser Glu Ser Met Asn Glu Thr Arg Leu 305 310 315 320	960
cga gaa atc ttt gga tgc tat ggg caa ata gtt tca gct aaa gtg atg Arg Glu Ile Phe Gly Cys Tyr Gly Gln Ile Val Ser Ala Lys Val Met 325 330 335	1008
tgt cat gag aat ggc aga agt aaa gga ttc ggc ttt gtg tgc ttc tct Cys His Glu Asn Gly Arg Ser Lys Gly Phe Gly Phe Val Cys Phe Ser 340 345 350	1056
aac tgt gaa gag tcc aaa cag gct aaa aga tat ctc aat ggg ttc tta Asn Cys Glu Glu Ser Lys Gln Ala Lys Arg Tyr Leu Asn Gly Phe Leu 355 360 365	1104
gtt gat gga aag cca ata gtt gtt cga gtt gca gag cgc aaa gag gat Val Asp Gly Lys Pro Ile Val Val Arg Val Ala Glu Arg Lys Glu Asp 370 375 380	1152
cga atc aag agg ttg cag caa tat ttt cag gca cag cca cgc cag tac Arg Ile Lys Arg Leu Gln Gln Tyr Phe Gln Ala Gln Pro Arg Gln Tyr 385 390 395 400	1200
acg caa gct cct tct gcc cct tca cca gct cag cca gtc ctc tca tat	1248

Thr	Gln	Ala	Pro	Ser 405	Ala	Pro	Ser	Pro	Ala 410	Gln	Pro	Val	Leu	Ser 415	Tyr		
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tat Tyr	tac Tyr	tat Tyr 435	atg Met	ggc	aat Asn	cag Gln	gtg Val 440	cca Pro	caa Gln	atg Met	tcc Ser	ggt Gly 445	cac His	caa Gln	aac Asn	1	344
atc Ile	acc Thr 450	acc Thr	tac Tyr	gtt Val	cca Pro	gct Ala 455	gly	aaa Lys	gtg Val	cct Pro	ctc Leu 460	Lys	gag Glu	aga Arg	aga Arg	. 1	.392
tca Ser 465	Met	cat His	ctg Leu	gtc Val	tac Tyr 470	aaa Lys	cat	ccg Pro	gct Ala	tat Tyr 475	ccc Pro	gtt Val	gcc Ala	aag Lys	agg Arg 480		L <b>44</b> 0
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gag Glu	gct Ala	gca Ala	aca Thr	Cys	tcc Ser	aaa Lys	gca Ala	aca Thr	Thr	tct Ser	gag Glu	gag Glu	aac Asn 510	Arg	aaa Lys		1536
gaa Glu	gaa Glu	cga Arg	Arg	ttg Leu	act Thr	ttg Leu	tca Ser 520	Gl3	aag Lys	ttg Lev	tca Sei	cca Pro 525	GIU	gtg Val	g aag L Lys		1584
gta Val	gag Glu 530	Glu	tca Ser	gga Gly	a aaa ⁄ Lys	caa Glr 535	Let	g caa i Glr	a tga 1								1614
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Ser Val His Leu Cys Arg Asn Ser Val Thr Gly Lys Ser Met Cys Tyr 50 55 60

- Ala Tyr Ile Asn Phe Asp Ser Pro Phe Ser Ala Ser Asn Ala Met Thr 65 70 75 80
- Arg Leu Asn His Ser Asp Leu Lys Gly Lys Ala Met Arg Ile Met Trp 85 90 95
- Ser Gln Arg Asp Leu Ala Tyr Arg Arg Arg Thr Arg Thr Gly Phe Ala 100 105 110
- Asn Leu Tyr Val Lys Asn Leu Asp Ser Ser Ile Thr Ser Ser Cys Leu 115 120 125
- Glu Arg Met Phe Cys Pro Phe Gly Ser Ile Leu Ser Cys Lys Val Val 130 135 140
- Glu Glu Asn Gly Gln Ser Lys Gly Phe Gly Phe Val Gln Phe Asp Thr 145 150 155 160
- Glu Gln Ser Ala Val Ser Ala Arg Ser Ala Leu His Gly Ser Met Val 165 170 175
- Tyr Gly Lys Lys Leu Phe Val Ala Lys Phe Ile Asn Lys Asp Glu Arg 180 185 190
- Ala Ala Met Ala Gly Asn Gln Asp Ser Thr Asn Val Tyr Val Lys Asn 195 200 205
- Leu Ile Glu Thr Val Thr Asp Asp Cys Leu His Thr Leu Phe Ser Gln 210 215 220
- Tyr Gly Thr Val Ser Ser Val Val Met Arg Asp Gly Met Gly Arg 225 230 235 240
- Ser Arg Gly Phe Gly Phe Val Asn Phe Cys Asn Pro Glu Asn Ala Lys 245 250 255
- Lys Ala Met Glu Ser Leu Cys Gly Leu Gln Leu Gly Ser Lys Lys Leu 260 265 270
  - Phe Val Gly Lys Ala Leu Lys Lys Asp Glu Arg Arg Glu Met Leu Lys 275 280 285

Gln Lys Phe Ser Asp Asn Phe Ile Ala Lys Pro Asn Met Arg Trp Ser 290 295 300

- Asn Leu Tyr Val Lys Asn Leu Ser Glu Ser Met Asn Glu Thr Arg Leu 305 310 315 320
- Arg Glu Ile Phe Gly Cys Tyr Gly Gln Ile Val Ser Ala Lys Val Met 325 330 335
- Cys His Glu Asn Gly Arg Ser Lys Gly Phe Gly Phe Val Cys Phe Ser 340 345 350
- Asn Cys Glu Glu Ser Lys Gln Ala Lys Arg Tyr Leu Asn Gly Phe Leu 355 360 365
- Val Asp Gly Lys Pro Ile Val Val Arg Val Ala Glu Arg Lys Glu Asp 370 375 380
- Arg Ile Lys Arg Leu Gln Gln Tyr Phe Gln Ala Gln Pro Arg Gln Tyr 385 390 395 400
- Thr Gln Ala Pro Ser Ala Pro Ser Pro Ala Gln Pro Val Leu Ser Tyr 405 410 415
- Val Ser Ser Ser Tyr Gly Cys Phe Gln Pro Phe Gln Val Gly Thr Ser 420 425 430
- Tyr Tyr Met Gly Asn Gln Val Pro Gln Met Ser Gly His Gln Asn 435 440 445
- Ile Thr Thr Tyr Val Pro Ala Gly Lys Val Pro Leu Lys Glu Arg Arg 450 455
- Ser Met His Leu Val Tyr Lys His Pro Ala Tyr Pro Val Ala Lys Arg 465 470 475 480
- Gly Ala Lys Gln Thr Leu Val Phe Lys Gly Glu Val Asn Arg Asn Leu 485 490 495
- Glu Ala Ala Thr Cys Ser Lys Ala Thr Thr Ser Glu Glu Asn Arg Lys 500 505 510
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					tct Ser											96
gac Asp	ggc Gly	gat Asp 35	gaa Glu	gcc Ala	gac Asp	ggt Gly	gag Glu 40	tct Ser	tct Ser	gct Ala	tcc Ser	gac Asp 45	gag Glu	aaa Lys	cgt Arg	144
gtt Val	gtc Val 50	cac His	ggc	gga Gly	gga Gly	gag Glu 55	aaa Lys	tcc Ser	atg Met	gag Glu	gag Glu 60	cta Leu	aat Asn	ttt Phe	tca Ser	192
gat Asp 65	tct Ser	gat Asp	aaa Lys	gaa Glu	tca Ser 70	acc Thr	ggt Gly	tgt Cys	caa Gln	tct Ser 75	ctc Leu	ccg Pro	gcg Ala	aca Thr	cct Pro 80	240
ccg Pro	aga Arg	cgg Arg	aga Arg	cgg Arg 85	cgg Arg	aga Arg	ggc	ggt Gly	gga Gly 90	gga Gly	gga Gly	gga Gly	tat Tyr	tta Leu 95	gcg Ala	288
gtg Val	agt Ser	tct Ser	ccg Pro 100	gtt Val	tcc Ser	ggc	gat Asp	aaa Lys 105	gct Ala	tac Tyr	gct Ala	agc Ser	gag Glu 110	aac Asn	gaa Glu	336
								Arg							ccg Pro	384
gag Glu	tgt Cys 130	cca Pro	ccg Pro	tgg Trp	gtt Val	gat Asp 135	agt Ser	atg Met	cgg Arg	agg Arg	agc Ser 140	Tyr	gtc Val	gga Gly	gat Asp	432

gaa Glu 145	cag Gln	agt Ser	agt Ser	cac His	ggt Gly 150	ggt Gly	tac Tyr	gga Gly	gga Gly	gga Gly 155	gtg Val	gtg Val	gtt Val	gtt Val	acg Thr 160	480
agg Arg	cct Pro	ata Ile	gga Gly	gga Gly 165	gga Gly	agg Arg	cca Pro	ttg Leu	tgt Cys 170	atg Met	gat Asp	tta Leu	gaa Glu	gaa Glu 175	gtc Val	528
aaa Lys	gct Ala	tgt Cys	aaa Lys 180	gat Asp	ttg Leu	gjå aaa	ttt Phe	gag Glu 185	ctt Leu	gaa Glu	ccg Pro	ggt Gly	cgg Arg 190	gtt Val	tcg Ser	576
tat Tyr	tcc Ser	999 Gly 195	tca Ser	acg Thr	gtg Val	gat Asp	act Thr 200	agt Ser	agt Ser	ggc	ggc	aat Asn 205	Ser	cct Pro	atc Ile	624
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Val Val His Gly Gly Glu Lys Ser Met Glu Glu Leu Asn Phe Ser 50 55 60

Asp Ser Asp Lys Glu Ser Thr Gly Cys Gln Ser Leu Pro Ala Thr Pro 65 70 75 80

Pro Arg Arg Arg Arg Arg Gly Gly Gly Gly Gly Tyr Leu Ala 85 90 95

Val Ser Ser Pro Val Ser Gly Asp Lys Ala Tyr Ala Ser Glu Asn Glu 100 105 110

Val Gln Lys Thr Asn Asn Asn Gln Arg Arg Arg Arg Leu Lys Pro 115 120 125

Glu Cys Pro Pro Trp Val Asp Ser Met Arg Arg Ser Tyr Val Gly Asp 130 135 140

Glu Gln Ser Ser His Gly Gly Tyr Gly Gly Gly Val Val Val Val Thr 145 150 155 160

Arg Pro Ile Gly Gly Gly Arg Pro Leu Cys Met Asp Leu Glu Glu Val 165 170 175

Lys Ala Cys Lys Asp Leu Gly Phe Glu Leu Glu Pro Gly Arg Val Ser 180 185 190

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212

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C: G:	ln	tcc Ser	cga Arg	tac Tyr	ttg Leu	ttc Phe 70	gca Ala	tta Leu	tca Ser	tgc Cys	ttc Phe 75	cag Gln	ato Met	gae : As	c ct p Le	eu .	ctc Leu 80	240
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a I	tc le	cca Pro	aat Asn	ggt Gly 100	gca Ala	gca Ala	ggc Gly	cat His	tac Tyr 105	ctt Leu	ctt Leu	gga Gly	a cti	t at u Il 11	.е т	ac	aag Lys	336
a	ag ys	aat Asn	gct Ala 115	Ala	caa Gln	caa Gln	ttt Phe	aaa Lys 120	cag Gln	tcc	ttg Lev	aca Thi	a at r Il 12	e As	c c	ct Pro	cta Leu	384
I	tt .eu	tgg Trp 130	Ala	gca Ala	tat Tyr	gag Glu	gaa Glu 135	Leu	tgt Cys	ata Ile	tta Lev	a gg 1 Gl 14	y Al	t go a Al	t g la G	gag 3lu	gaa Glu	432
7	gca Ala L45	Thr	gca Ala	a gtt a Val	ttt L Phe	ggt Gly 150	Glu	aca Thr	gct	gct Ala	cto Let 15	u se	c at	t ca .e G	aa a ln 1	aag Lys	cag Gln 160	480
•	tat Tyr	ato Met	g caa Gli	a caa n Gl	a cto n Leo 16	ı Sei	a act	tcc Ser	cto Lev	gg Gly 170	, re	a aa u As	c ac n Th	et t	yr .	aac Asn 175	gag Glu	528
,	gaa Glu	cgi Ar	t aat g Asi	t tc n Se 18	a act r Th	t tct r Sei	act Thi	aaa Lys	aac Asi 189	1 Th	g ag r Se	t to r Se	et ga	IU A	at sp 90	tat Tyr	agt Ser	576
	cca Pro	ag Ar	g ca g Gl 19	n Se	t aa r Ly	a cad s Hi	c aca s Thi	a caa c Glr 200	ı Se:	c ca r Hi	t gg s Gl	jc ct y Le	en Ti	aa g ys A 05	at	atc Ile	tcc Ser	624
	gga Gly	a aa 7 As 21	n Ph	c ca e Hi	t tc s Se	t ca r Hi	t gga s Gl	y Vai	t aa l As	t gg n Gl	a gg y Gl	Ly Va	tt t al S 20	cg a er Æ	ac Asn	at <u>c</u> Met	tca Ser	672
	tto Pho	е Ту	t aa r As	t ac	g cc ır Pr	t tc o Se 23	r Pr	a gt o Va	g gc l Al	t go a Al	a G.	ag c ln L 35	ta t eu S	cc g er (	ggt 31y	ata Ile	a gct e Ala 240	720
	cc. Pr	a co o Pr	a co co Pr	ea ct	t tteu Ph	ie Ar	g aa g As	t tt n Ph	t ca e Gl	g co n Pr 25	O A	ct g la V	tt g	ca a	aac Asn	Pro 25	a aac o Asn 5	768
	tc Se	c ct r Le	et at	le Ti	et ga ir As	ac ag sp Se	jt to er Se	t cc r Pr	a aa o Ly 26	s Se	cc a er T	ct g hr V	tt a Val 1	ASD	tct Ser 270	111	t ctt r Lev	: 816 I
	са	a go	ca C	ct a	ga ag	ga aa	ag tt	t gt	a ga	at g	aa g	ga a	ag 1	tta	cgt	aa	g att	864

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tct Ser 305	gct Ala	gat Asp	tca Ser	gjå aaa	gca Ala 310	aac Asn	att Ile	aat Asn	tca Ser	agt Ser 315	gtt Val	gca Ala	aca Thr	gta Val	ag Se 32	I	960
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ato Ile	aca Thi	a att	ggt Gly	gtt Val	. Ser	gaa Glu	att Ile	tta Leu	aac Asn 410	Leu	ctt Lei	agg 1 Arg	g aca	t Ct Le 41	u	ga Hy	1248
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ac _s Th	g ta r Ty:	t ate	t Lys	a ctt s Lei	cca 1 Pro	cat His	aag Lys	s His	tat Tyr	aat Asr	aca n Th	a gga r Gly 44	y TI	g gt p Va	t d	ctt Leu	1344
tc Se:	c ca r Gl 45	n Va	c ggg 1 Gl	g aaa y Ly:	a gca s Ala	tac Tyr 455	Ph	t gaa e Glu	a cta u Lev	att 1 Ile	t ga e As 46	р ту	t tt r Le	a ga u Gl	ig 9 lu 1	gct Ala	1392
ga Gl 46	u Ly	g gc s Al	a tt a Ph	c cg e Ar	t ctt g Lei 470	ı Ala	c cg	t ctg g Le	g gct u Ala	tci a Se: 47	r Pr	t ta o Ty	t tg r Cy	c tt	eu '	gaa Glu 480	1440
G1 99	a at y Me	g ga t As	t at p Il	a ta e Ty 48	r Se	ace Thi	g gt r Va	c ct l Le	c tar u Ty: 49	r Hi	t tt s Le	g aa eu Ly	g ga 's Gl	u A	ac sp 95	atg Met	1488
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cc	t ca	aa to	t tg	ıg tg	t gc	t at	g g9	ja aa	ıt tg	c ta	ıt aç	gc tt	g ca	aa a	ag	gac	1584

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aga Arg 545	ttt Phe	gca Ala	tat Tyr	gca Ala	cat His 550	acc Thr	tta Leu	tgt Cys	ggc Gly	cac His 555	gaa Glu	tac Tyr	aca Thr	act Thr	ctt Leu 560		1680
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gag Glu	gag Gli	g cto Let 67!	ı Ly:	a gag s Gli	g tat ı Tyı	gcg Ala	g cc a Pro 68	o Se	a ga r Gl	g ag u Se	c ag r Se	c gt r Va 68	т ту	c go	t tt la Le	a u	2064
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cat His 70!	s Ph	c gg e Gl	t ct y Le	a gc u Al	t tta a Le	u As	t at p Me	g aa t Ly	a co	g cc o Pr 71	LA O	ca ac la Tì	et ga ur As	ac g	tt go al Al 72	.a.	2160
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Asn Gln Ala Tyr Ser Ala Tyr His Leu Leu Lys Gly Thr Gln Met Ala 50 55 60

Gln Ser Arg Tyr Leu Phe Ala Leu Ser Cys Phe Gln Met Asp Leu Leu 65 70 75 80

Asn Glu Ala Glu Ser Ala Leu Cys Pro Val Asn Glu Pro Gly Ala Glu 85 90 95

Ile Pro Asn Gly Ala Ala Gly His Tyr Leu Leu Gly Leu Ile Tyr Lys 100 105 110

Lys Asn Ala Ala Gln Gln Phe Lys Gln Ser Leu Thr Ile Asp Pro Leu 115 120 125

Leu Trp Ala Ala Tyr Glu Glu Leu Cys Ile Leu Gly Ala Ala Glu Glu 130 135 140

Ala Thr Ala Val Phe Gly Glu Thr Ala Ala Leu Ser Ile Gln Lys Gln 145 150 155 160

Tyr Met Gln Gln Leu Ser Thr Ser Leu Gly Leu Asn Thr Tyr Asn Glu 165 170 175

Glu Arg Asn Ser Thr Ser Thr Lys Asn Thr Ser Ser Glu Asp Tyr Ser 180 185 190

Pro Arg Gln Ser Lys His Thr Gln Ser His Gly Leu Lys Asp Ile Ser 195 200 205

- Gly Asn Phe His Ser His Gly Val Asn Gly Gly Val Ser Asn Met Ser 210 215 220
- Phe Tyr Asn Thr Pro Ser Pro Val Ala Ala Gln Leu Ser Gly Ile Ala 225 230 235 240
- Pro Pro Pro Leu Phe Arg Asn Phe Gln Pro Ala Val Ala Asn Pro Asn 245 250 255
- Ser Leu Ile Thr Asp Ser Ser Pro Lys Ser Thr Val Asn Ser Thr Leu 260 265 270
- Gln Ala Pro Arg Arg Lys Phe Val Asp Glu Gly Lys Leu Arg Lys Ile 275 280 285
- Ser Gly Arg Leu Phe Ser Asp Ser Gly Pro Arg Arg Ser Ser Arg Leu 290 295 300
- Ser Ala Asp Ser Gly Ala Asn Ile Asn Ser Ser Val Ala Thr Val Ser 305 310 315 320
- Gly Asn Val Asn Asn Ala Ser Lys Tyr Leu Gly Gly Ser Lys Leu Ser 325 330 335
- Ser Leu Ala Leu Arg Ser Val Thr Leu Arg Lys Gly His Ser Trp Ala 340 345 350
- Asn Glu Asn Met Asp Glu Gly Val Arg Gly Glu Pro Phe Asp Asp Ser 355 360 365
- Arg Pro Asn Thr Ala Ser Thr Thr Gly Ser Met Ala Ser Asn Asp Gln 370 375 380
- Glu Asp Glu Thr Met Ser Ile Gly Gly Ile Ala Met Ser Ser Gln Thr 385 390 395 400
- Ile Thr Ile Gly Val Ser Glu Ile Leu Asn Leu Leu Arg Thr Leu Gly
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- Glu Gly Cys Arg Leu Ser Tyr Met Tyr Arg Cys Gln Glu Ala Leu Asp 420 425 430

Thr Tyr Met Lys Leu Pro His Lys His Tyr Asn Thr Gly Trp Val Leu 435 440 445

- Ser Gln Val Gly Lys Ala Tyr Phe Glu Leu Ile Asp Tyr Leu Glu Ala 450 455 460
- Glu Lys Ala Phe Arg Leu Ala Arg Leu Ala Ser Pro Tyr Cys Leu Glu 465 470 475 480
- Gly Met Asp Ile Tyr Ser Thr Val Leu Tyr His Leu Lys Glu Asp Met 485 490 495
- Lys Leu Ser Tyr Leu Ala Gln Glu Leu Ile Ser Thr Asp Arg Leu Ala 500 505 510
- Pro Gln Ser Trp Cys Ala Met Gly Asn Cys Tyr Ser Leu Gln Lys Asp 515 520 525
- His Glu Thr Ala Leu Lys Asn Phe Leu Arg Ala Val Gln Leu Asn Pro 530 540
- Arg Phe Ala Tyr Ala His Thr Leu Cys Gly His Glu Tyr Thr Thr Leu 545 550 555 560
- Glu Asp Phe Glu Asn Gly Met Lys Ser Tyr Gln Asn Ala Leu Arg Val 565 570 575
- Asp Thr Arg His Tyr Asn Ala Trp Tyr Gly Leu Gly Met Ile Tyr Leu 580 585 590
- Arg Gln Glu Lys Leu Glu Phe Ser Glu His His Phe Arg Met Ala Phe 595 600 605
- Leu Ile Asn Pro Ser Ser Ser Val Ile Met Ser Tyr Leu Gly Thr Ser 610 620
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Met Gly Arg Ile Tyr Lys Arg Arg Asn Met His Asp Lys Ala Met Leu 690 695 700

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